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## Original Communications

### THE PROBLEM OF THE HIATUS HERNIA OF THE DIAPHRAGM


CONRAD R. LAM, M.D., AND LEO J. KENNEY, M.D. (BY INVITATION)
DETROIT, MICH.


THE problem of the hiatus hernia of the diaphragm is actually twofold. One aspect is represented by the dilemma of the internist who must advise the patient in whom this hernia has been demonstrated. This patient may be told to "forget it," or to change his habits of eating and sleeping and to take palliative drugs in an attempt to make the situation tolerable, or he may be advised to consult a surgeon about an operation. The other part of the problem is that faced by the surgeon, who, in the face of conflicting advice, must choose and carry out an operative procedure. So great has been the confusion with regard to technical details and so far from ideal have been the results from the methods actually selected that the perplexity of the internist is understandable. Obviously what is needed is a standard curative operation which can be used by any thoracic surgeon on practically any patient with hiatus hernia of the diaphragm. It is our belief that such an operation is currently available and that it should be employed to the exclusion of all others.

Naturally, the logical plan of operative treatment of hiatus hernia would include reduction of the herniated structures back into the abdominal cavity and closure of the aperture to maintain this reduction. There have been reports of large series of cases repaired by the transabdominal[1] and transthoracic[2, 3] routes. Although these authors have indicated that in their hands these procedures have not been associated with an important recurrence rate, others[4, 5] have reported a discouraging number of failures. In fact, several authors have advised that attempts at definitive repair are not worth while and that it is preferable to enlarge rather than diminish the hernia orifice, so that the stomach is not constricted.[6, 7] A similar attitude of defeatism is represented by those who recommend interruption of the phrenic nerve.[8]


From the Department of Surgery of the Henry Ford Hospital.



Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.





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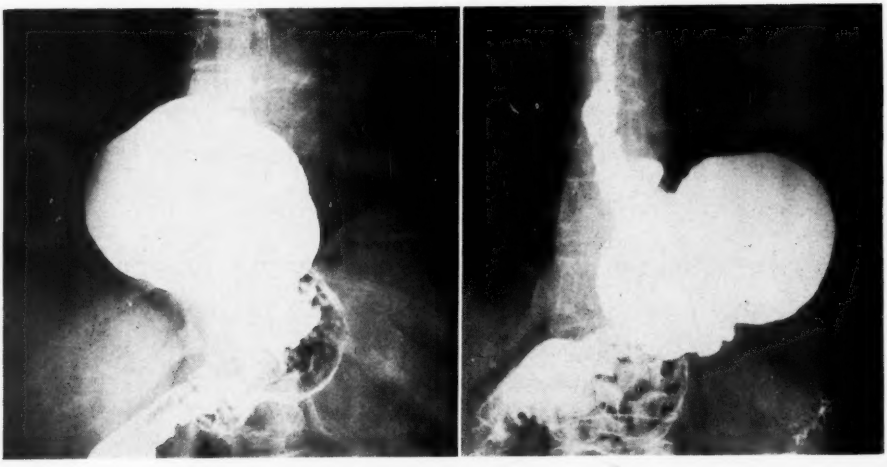
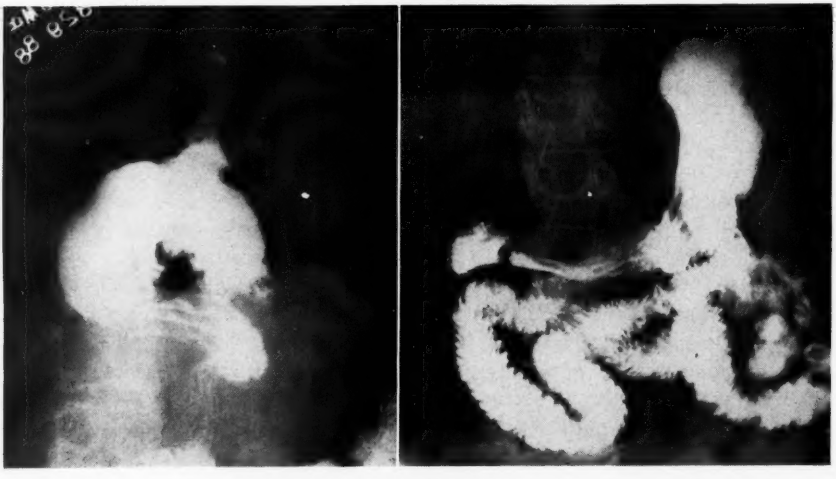
In an early series of eighteen patients with repair of hiatus hernia by the transthoracic approach by one of us (C. R. L.), there was a discouraging number of recurrences. At least six had roentgen evidence of recurrence, of which four had return of symptoms and two had second operations. An example of rather prompt recurrence is shown in the roentgenograms in Figs. 1 and 2. This



*A.* *B.*

Fig. 1.—*A*, Preoperative roentgenogram of large hiatal hernia. The central location in the mediastinum is striking. *B*, Postoperative roentgenogram taken five weeks after repair by unsatisfactory technique. The beginning of recurrence is evident.



*A.* *B.*

Fig. 2.—*A*, Roentgenogram of patient shown in Fig. 1, four years later, showing large recurrence with upside down stomach. *B*, Roentgenogram after second repair of hiatal hernia by recommended method (eight months postoperative).

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experience led us to the logical conclusion that there was some fundamental defect in the method of repair which was being utilized. The technique employed in this unfortunate series might be summarized as follows: 1. The hernia was exposed through an incision through the left eighth interspace and an attempt was made to obliterate the peritoneal sac by excision and/or plication.

Fig. 3.—Artist's drawing of inferior surface of diaphragm. Herniation through the esophageal hiatus occurs after lengthening and widening of the posteroinferior part of the aperture.

2. The size of the hernial orifice was reduced by the placing of sutures in the most accessible location, which was usually at the anterolateral portion of the circumference of the hiatus. At least two authors[1, 2] had described the esophageal hiatus as being frequently a transverse slit, which could be closed by placing sutures to the right, to the left, or on both sides of the esophagus.

It is our opinion that the true long axis of the esophageal hiatus lies in the sagittal plane and that an anteroposterior suture line behind the esophagus is the most effective. Merendino, Varco, and Wangensteen,[9] Allison[10] of Leeds, and Effler and Ballinger[11] came to the same conclusion. Each of these three excellent papers contains directions for an anatomically sound repair of uncomplicated hiatus hernia by the approximation of the crura behind the esophagus. However, in two of them[9, 11] attention was probably diverted from this important matter by the emphasis which was given in the titles and the bodies

Fig. 4.—Artist's drawing of superior surface of the diaphragm. Herniation occurs through the area occupied by the crural membrane.

of the papers to the problem of the so-called short esophagus and the necessity of incising the diaphragm out toward the dome for the transplantation of the esophagus laterally and anteriorly.

To supplement the anatomic information obtained during operation on patients with hiatus hernia, we made dissections of the diaphragms in eight cadavers, and drawings were made.*

*By Mr. Elton Hoff, medical artist.

The crura of the diaphragm take origin from tendinous attachments that arise from the anterolateral surfaces of the bodies of the first three lumbar vertebrae. The fibers become muscular and surround the aorta at the level of the celiac axis. These muscular bundles pass upward in an interlocking manner soon separating to form the esophageal hiatus. They then insert into the middle leaf of the central tendon.

The inferior surface of the diaphragm is illustrated in Fig. 3. The right crus is made up of muscle that originated from both the right and left sides of the vertebral bodies and a similar situation exists in the formation of the left crus. The medial and lateral margins of the esophageal hiatus consist of those fibers that took origin contralaterally. On the thoracic surface (Fig. 4) the crura exhibit the same decussating phenomena.

The anterior margin of the esophageal hiatus consists of unyielding tendinous tissue of the middle leaflet of the central tendon. The posterior aspect of the hiatus is notably free of any firm structure. In every dissected specimen the area posterior to the esophagus consisted of a triangular space that was bridged by a thin areolar membrane. This is designated as the crural membrane in Fig. 4. It is at this site that the abdominal contents find their way into the mediastinum creating a hiatus hernia. We are convinced that obliteration of this anatomically weak area is of primary importance in the repair of this hernia.

In addition to the anatomic studies, we carried out some physiologic studies on the effect of phrenic nerve stimulation on the musculature of the diaphragm. When the fingers were placed in the enlarged hiatus of a patient with hernia and the phrenic nerve was stimulated mechanically or by faradic current, there was retraction of the dome of the diaphragm, but no tendency to contraction of the crura forming the rim of the hernial orifice. In the experimental animal (dog), stimulation of the phrenic nerve did not cause the left crus to contract (Fig. 5). Measurements of the pressure in a hydrostatic bag placed in the esophageal hiatus showed only slight increase in pressure when the phrenic nerve was stimulated (Fig. 6).

Relaxation of the hiatus after section of the phrenic nerve could not be demonstrated. These observations suggest that concomitant paralysis of the left phrenic nerve is of no value in the procedure of hiatal herniorrhaphy, and that it may actually do harm since postoperative pulmonary complications may be induced by the depression of respiratory function. It has been difficult logically to explain the palliation which has been reported in some patients who have had phrenic nerve interruption for hiatus hernia, although it has been assumed that the "spasm" of the hiatus is relieved.[8] Amendola[12] recently has made an observation which may explain some of the instances of symptomatic benefit after phrenic paralysis. Permanent phrenic interruption had been carried out on an elderly woman, with the result that the diaphragm rose high on the left chest, pulling the fundus of the stomach with it and thus reducing the hernia. However, the esophagus became so angulated where it passed around the muscular ring that dysphagia appeared, and it was necessary to operate and transplant the esophagus anteriorly and laterally to the dome of the diaphragm.

The procedure which we recommend for the repair of hiatus hernias of the diaphragm is as follows: The lower left thoracic cavity is entered through a posterolateral incision through the seventh interspace. The pleura overlying the esophagus (pulmonary ligament) is divided to permit a tape to be passed around the esophagus (Fig. 7). The pleural covering of the herniated stomach and retroperitoneal fat is brushed off to expose the muscular edge of the hiatus.

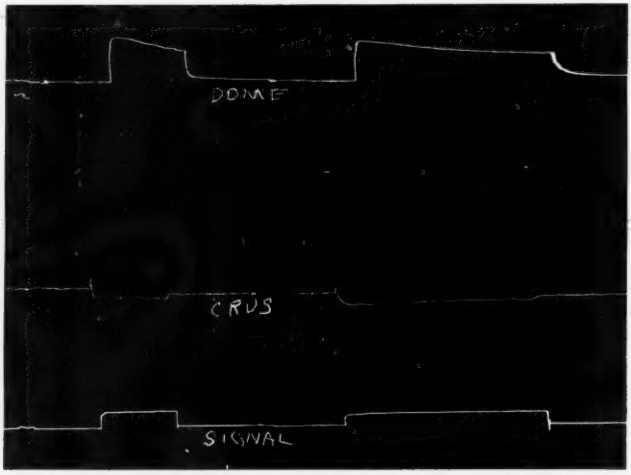



Fig. 5.—Kymograph record showing motion of dome of diaphragm and lack of motion of left crus during stimulation of left phrenic nerve. The writing points were activated by strings passing superiorly from the two parts of the diaphragm.

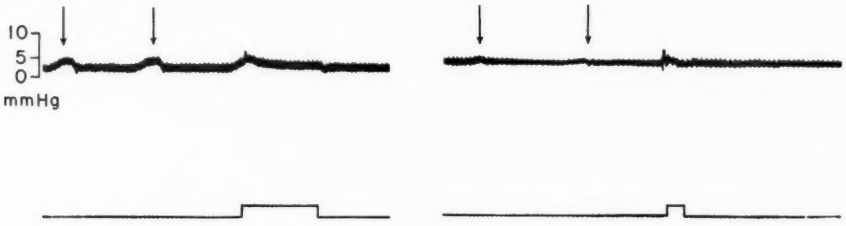



Fig. 6.—Pressure recordings from a hydrostatic bag placed in the esophageal hiatus of the dog (Hathaway apparatus). The record on the left shows the slight pressure fluctuations of normal inspiratory movements (arrows). Sustained faradic stimulation of the left phrenic nerve (lower signal) caused no greater fluctuation. The record on the right shows that no relaxation was produced by section of the phrenic nerve (signal).

A small incision is made in the dome of the diaphragm and a long clamp is passed intraperitoneally along the under surface of the diaphragm to pierce the peritoneum near the anterior surface of the hiatus and emerge from the hiatus. This clamp grasps the tape which encircles the esophagus and draws it out of the opening in the diaphragm. During the subsequent repair, traction on this tape assists greatly in maintaining reduction and providing exposure for the suturing of the crura (Fig. 8). The esophagus is easily displaced anteriorly after the division of a small amount of areolar tissue and a vessel or two.

Fat and areolar tissue are cleaned off the right crus so that sutures can be placed accurately. However, it is the palpating finger which actually guides the placement of these sutures. It will be found that the medial portion of the

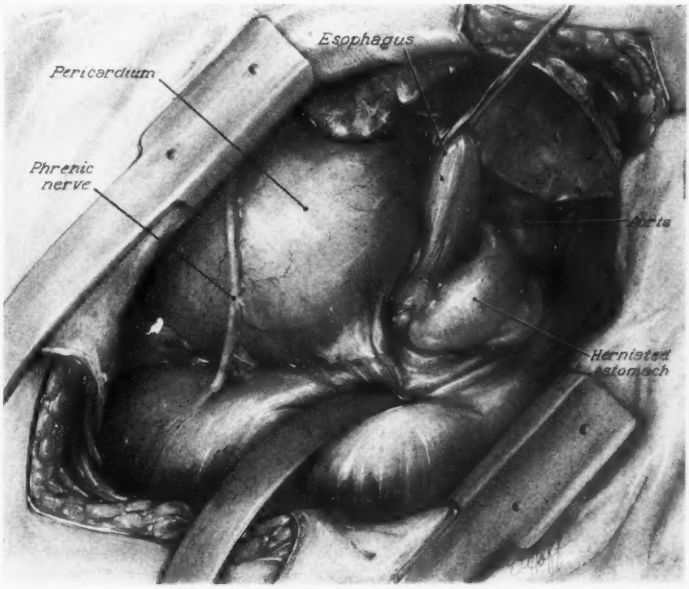



Fig. 7.—Exposure of hiatal hernia through left posterolateral seventh interspace incision.

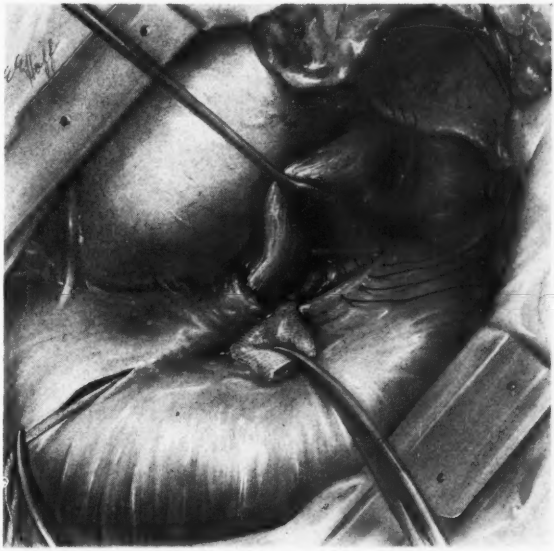


Fig. 8.—The essential step in the repair of hiatus hernia; the placing of sutures through the crura posterior to the esophagus. Note the tape passed around the lower end of esophagus and through a small opening in the dome of the diaphragm which helps to maintain reduction.

orifice (commonly called the right crus) is fibrous and tough and holds sutures well, while the lateral portion (left crus) is composed mainly of muscle and there is a tendency for sutures to tear out. To obviate this, the sutures should pass through all layers of the diaphragm, including the diaphragmatic pleura.

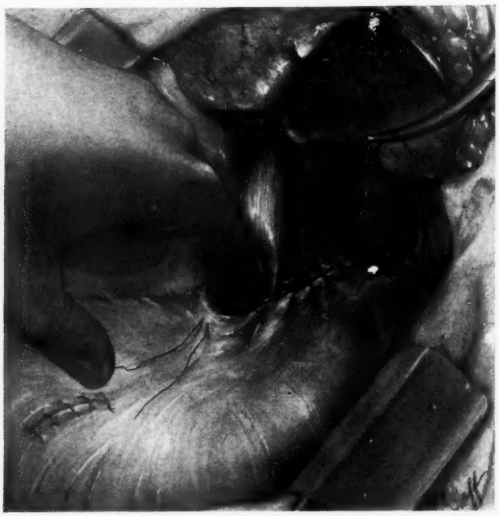


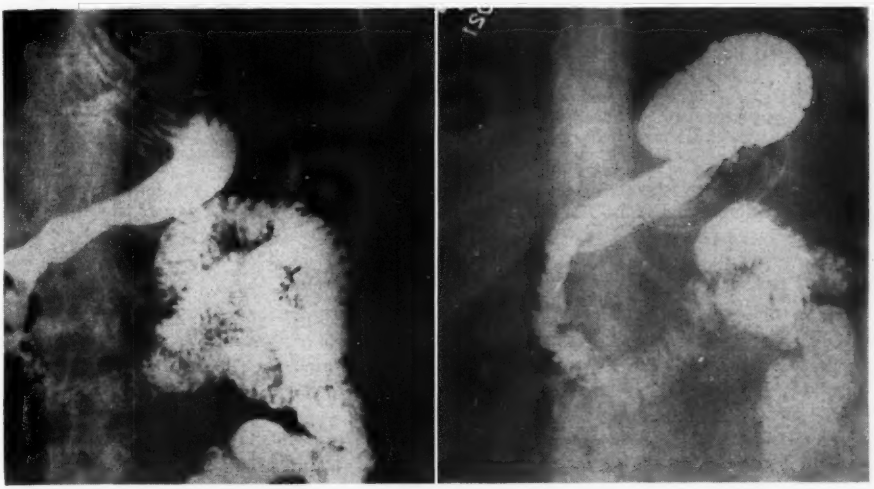
Fig. 9.—Final closure of esophageal hiatus with finger inserted to prevent too light closure. The small incision in the dome of the diaphragm has been closed.

Usually five or six sutures placed posterior to the esophagus are all that are necessary. Before these sutures are tied, three or more mattress type sutures are placed which attach the esophageal musculature to the under surface of the esophageal hiatus. These sutures correspond to those which Allison recommends for the fixation of the so-called phrenoesophageal ligament to the under surface of the diaphragm. The posterior sutures are then tied; a finger is inserted in the orifice by the side of the esophagus as the most anterior one is tied (Fig. 9). No dysphagia has been produced when this precaution has been observed in determining the size of the opening.

It will be noted that no attempt was made to excise or plicate the peritoneal sac, if one existed. It is our opinion that since this lesion is a sliding hernia, no useful purpose is served in removing a small amount of peritoneum on one side of the sac.

Since the above technique was adopted, twenty hernias have been repaired. In preparation for this report, all patients were recalled, questioned for symptoms of recurrence and submitted to roentgen examination. The follow-up period on nine cases was from one to two years, and in six others was from six months to one year. In no instance has there been roentgen evidence of recurrence (Fig. 10). Seventeen patients are asymptomatic. Two of the others had

persistence of dysphagia from pre-existing esophagitis and are improved following dilatation. Another patient with recurrence of gastrointestinal symptoms has recently undergone cholecystectomy for cholelithiasis.



*A.* *B.*

Fig. 10.—*A*, Preoperative roentgenogram of hiatal hernia of moderate size. *B*, Postoperative roentgenogram following repair by recommended method (seven months after operation).

There has been no mortality in the thirty-eight patients with transthoracic repair of hiatus hernia. Aside from the recurrences in the early group, there has been no morbidity of note with the exception of one patient who developed a large hemothorax which became infected after a number of thoracenteses. Drainage by rib resection was necessary.

We have not observed a case of so-called "short esophagus" which would have necessitated a deviation from the technique described.

## SUMMARY

The unsatisfactory general status of surgical treatment of esophageal hiatus hernia of the diaphragm has been described. This appears to be due to lack of standardization of the definitive operation. An anatomically sound repair with closure of the opening by sutures placed posterior to the esophagus as recommended by previous authors appears to give the best promise of success.

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## DISCUSSION

DR. ALEXANDER E. W. ADA, New York.—I enjoyed the careful review and critical appraisal of the various surgical procedures for the treatment of hiatus hernia, as presented by Drs. Lam and Kenney. The multiplicity of operations and the high percentage of failures attest to the confusion that prevails today in the treatment of this lesion. It explains in some part the reticence of our medical confreres in recommending surgical therapy. Past experience, coupled with an honest scrutiny of our results, indicates that uniform success attends the procedure recommended by Allison and the anterior transplantation of the esophagus suggested by Wangensteen. The following case illustrates the result obtained by these combined techniques:

This patient was 65 years of age and came to me in 1949 because of a massive gastric hemorrhage.

(Slide.) This is a lateral x-ray view of the chest showing the entire stomach with the exception of the pylorus to be within the thorax and (slide) the barium enema shows that part of the transverse colon was present in the hernia sac.

An Allison repair with anterior transplantation of the esophagus produced a satisfactory end result. A small, oblique incision of sufficient size to admit the assistant's hand was required in the left upper abdomen in order to maintain the stomach within the abdomen during the repair of the diaphragm.

(Slide.) This film was taken some time after operation, following a barium swallow. You can readily see the left leaf of the diaphragm with the cardia of the stomach in its normal position, and also see that there is no recurrence of the hernia.

We have observed esophagitis in varying stages as an associated disease. The etiology of this lesion remains controversial. We have resected the esophagus and performed an esophagogastrostomy in four such cases with one death.

(Slide.) This x-ray film after the ingestion of barium depicts the advanced stage of the disease which we interpret as hypertrophic esophagitis with stenosis.

Our last patient, operated on two months ago for this lesion, had previously undergone an Allison repair for a recurrent hiatus hernia in 1950. We thought that the esophagitis that existed at that time was reversible as it did not appear to involve the entire wall of the esophagus. Despite the cure of the hernia the esophagitis progressed, an ulcer perfortaed into the mediastinum with mediastinitis and there were two episodes of massive hemorrhage. This case was successfully completed by performing a Lewis operation in one stage. Through a midline abdominal incision, the stomach was mobilized, maintaining circulation from the right gastric and right gastroepiploic arteries. The patient was then turned on the left side and the right thorax was opened through the sixth rib bed. The lower half of the esophagus was resected and an intrathoracic-esophagogastrostomy was completed. To date the result has been satisfactory.

DR. E. K. JOHNSON, New York.—I think that the problem of herniation through the esophageal hiatus has been very clearly presented by Drs. Lam and Kenney. I rise only because we have seen this condition in the newborn infant, and until then I was unaware of the possibility. The first case was that of a newborn infant with obstructive symptoms of regurgitation and vomiting. The diagnostic procedure for atresia of the esophagus of passing a small catheter into the esophagus was employed. Radiopaque oil was instilled into the catheter and the fluoroscopist reported a small pocket above the diaphragm. The symptoms of obstruction abated and no surgery was performed. In the next case similar symptoms had occurred and the diagnostic procedure was repeated. About ten hours later the infant started swallowing normally. The roentgenogram revealed a hiatus hernia. In the third case with similar symptoms the diagnostic procedure demonstrated a hiatus hernia.

(Slide.) At your left is the lateral roentgenogram showing radiopaque material in the esophagus and in the herniated portion of the stomach. To the right is an anteroposterior roentgenogram showing air-filled viscus in the mediastinum back of the heart shadow.

The hernia was repaired by a transabdominal approach, as I was uncertain of the diagnosis. The elastic pleural-esophageal membrane described by Dr. Kenney had herniated on the right side and the left lobe of the liver projected upward into that space. A small loop of bowel was also present, but I do not believe it was there normally. The repair was similar to that Dr. Kenney has described, by displacing the esophagus in an anterolateral direction and bringing the two crura of the diaphragm together. The repair seemed secure.

We have a complete record of our case, since at the end of one month of life, the infant was found dead, evidently from suffocation by crib blankets. An autopsy showed that the diaphragm was normal, the repair had held securely and there was no apparent shortening of the esophagus.

We believe these patients might be of some interest because it was thought they had atresia of the esophagus. The diagnosis was clearly established by the catheter radiopaque oil method. I do not know why the first two infants were relieved of symptoms and the third continued to be obstructed unless, as has been stated, an associated esophagitis may be the cause.

DR. RICHARD H. SWEET, Boston.—I was impressed by Dr. Kenney's beautiful drawings of the anatomic situation which he found, but they rather surprised me because I have almost never found such a situation at operation, as demonstrated there. In all the patients, some 150 or more, that I now have had experience with, there is always a sac in the first place. This sac is always anterior. I have never seen a peritoneal sac posterior, and I do not see how anatomically it could exist there. There is, however, often a bulge of the stomach posteriorly without a true sac behind. The sac is always in front, embracing the portion of the stomach that has slid up through the hiatus but not completely. It never surrounds it, as it appears to do in Allison's drawings, for example. Although I agree completely with him in the principles he has elaborated, his drawings are misleading because they allow one to believe that the hernia sac completely encircles the stomach, which it does not do and which it cannot do.

I certainly agree with Dr. Lam and Dr. Kenney that the posterior approximation of the margins of the diaphragm at the hiatus is the important thing, but I find also that the direction and the configuration of the hiatus are exceedingly variable. Sometimes it is exactly U-shaped with a smooth rounded border. Sometimes it is elliptical, and although one feels that the posterior sutures are the more important, occasionally I find it necessary to use a few sutures in the front, mostly to the right in this elliptical type of aperture. This is of importance, I believe, because in one of the patients I had with recurrence, although the integrity of the hiatus remained, there was a recurrence up under the pericardium, in this little triangular defect which is sometimes seen. These are always sliding hernias.

One other point which I think is worthy of comment, which Dr. Harrington might have brought up if he were here, is that if one is fearful of the sutures tearing loose, which I

doubt very much if heavy suture material is used, it is a great help to use strips of fascia taken from the patient's left thigh.

DR. EARLE B. KAY, Cleveland.—I have employed a somewhat similar technique in the surgical repair of more than 100 patients with hiatal hernias since 1942. Several factors, however, regarding both the etiology and surgical treatment of hiatal hernias should be further stressed. One of the factors responsible for development of a hiatal hernia is the presence of an atrophic or redundant diaphragmatic esophageal ligament. This ligament was first described by Laimer in 1883. It arises on the under surface of the diaphragm, divides into two limbs, and the ascending one goes through the hiatal opening and attaches to the esophagus. It is the antagonist of the longitudinal musculature of the esophagus and normally prevents the stomach from herniating into the chest upon esophageal contraction. I believe that after the redundant hernial sac and ligament are excised, this ligament should be again sewn to the esophagus during the reconstruction of this area.

In addition to the above, as the surgeon explores patients with hiatal hernias, it will be noted that the herniated stomach is invariably anterior. In my experience there appears to be considerably less diaphragmatic muscle posteriorly between the esophageal and aortic hiatus than what one encounters normally, and this is a definite factor in producing the enlarged esophageal stoma. This is why it is important to approximate the crura posteriorly by two to three sutures and fashion a new diaphragmatic shelf between these two hiatal openings. This in itself will completely reduce the size of the enlarged esophageal stoma.

DR. R. A. RASMUSSEN, Grand Rapids.—I rise simply to mention a maneuver which Dr. Harrington and others have used. We have used it with success and we feel that it may be of some importance. That is, to open the diaphragm more than was shown and to suture the cardia of the stomach to the under surface of the diaphragm, thereby anchoring it at that point.

DR. ROBERT M. JANES, Toronto.—I am sorry Dr. Harrington is not here, but I think someone ought to say that it is the principle and the adequacy of the repair that are important and that a satisfactory repair can be accomplished through an abdominal approach as well as through a thoracic approach. When there is an associated abdominal condition it may be worth while to be familiar with an abdominal as well as a thoracic approach.

I was interested in Dr. Sweet's remarks about fascia. It recalls a rather amusing incident to me. I think perhaps I published a report about the first repair with fascia; it was a long time ago when my then chief, Dr. Gallie, was unfamiliar with the approach through the chest. I opened the chest, he repaired the diaphragm with fascia, and then I closed the chest in this very complicated operation.

DR. LAM (Closing).—Dr. Kenney and I appreciate the discussion. Dr. Ada's case was very interesting and Dr. Johnson's was especially so since we have come to believe that this disease is one of rather obese women in their 50's rather than in the newborn infant. Dr. Sweet's experience of course is classic. In our attempt to call attention to the posterior part of this hernia, we have more or less de-emphasized the fact that there is a portion of the peritoneal sac anteriorly. Our first illustration showed the herniated structures after they had been partly dissected out. Since we do not open the peritoneum and pay no attention to the sac, we sometimes do not know whether or not a sac is present.

Dr. Kay mentioned the Allison sutures. Of course, we use these, giving some attention to the so-called phrenoesophageal ligament by the placement of several stitches which approximate the esophagus to the diaphragm. We appreciate the remarks of Dr. Rasmussen and Dr. Janes.

It has been our feeling that too much attention has been paid to the peritoneal sac and that surgeons have become fatigued from trying to suture this very friable sort of material. If one conserves energy and neglects this sac, giving special care to the posterior sutures, better results may be expected.

# MUSCLE WALL TUMORS OF THE ESOPHAGUS

RICHARD H. SWEET, M.D., LAMAR SOUTTER, M.D., AND CARLOS TEJADA VALENZUELA, M.D. (BY INVITATION)
BOSTON, MASS.

DURING the past ten years, as the techniques of esophageal surgery have improved, there has been a steadily increasing interest in esophageal tumors. The benign neoplasms and the sarcomas of the esophagus reported in the literature have been completely summarized a number of times.[1-5] It would be redundant to repeat here what has been carefully recorded before. Instead, this paper deals primarily with our own series of twenty benign and two malignant muscle wall tumors observed over a twenty-year period. The pathologic considerations, clinical symptoms, and surgical therapy of these growths are discussed and correlated as far as possible with those previously reported.

## CONSIDERATIONS OF PATHOLOGY AND GROWTH

Esophageal tumors can be divided according to the layers in which they arise. Carcinomas and certain polyps arise primarily from the mucosa. Cysts, certain sarcomas, pedunculated fibromyxomas, and lipomas are among those which grow in the submucosa. Leiomyomas, neurofibromas, fibromas, fibromyomas, leiomyosarcomas, fibrosarcomas, and rhabdomyosarcomas originate in the muscularis.

*1. Benign Tumors.*—The benign muscle wall tumors have little to distinguish them one from another on the basis of their clinical behavior. They are often difficult to distinguish microscopically because of a similarity of cellular pattern unless special smooth muscle-cell stains are employed. In reviewing the slides of the tumors presented in this series, new sections were cut from many and both Masson and phosphotungstic acid stains were used for more precise histologic identification. On the basis of these studies, seventeen of the twenty benign tumors presented here were found to be leiomyomas*; two were diagnosed as neurofibromas; and one was identified as a fibromyoma. Two which had previously been called neurofibroma were firmly established as leiomyomas. It is of some interest that one of these has repeatedly appeared in various articles as a neurofibroma excised by Dr. Churchill.[6] Actually, it was probably the first leiomyoma of the esophagus to be removed surgically in this country.

All of these benign growths are firm, well-circumscribed, but not necessarily encapsulated tumors. Although they may become firmly adherent to surrounding tissues, they are not invasive. They occasionally show areas of metaplasia and possibly can develop malignant degeneration. One tumor in

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*Two of these tumors have been reported from clinicopathologic conferences at the Massachusetts General Hospital but are not included in any series of cases reported to date.[36, 37]

our series had become partially cystic, two more had become partially calcified. At least six tumors have been reported in the literature as showing calcification.[4, 7] Ulcerations of the mucosa over a tumor are rare unless it extends into the stomach. One of our patients had multiple, small esophageal ulcers and a large crater partially in the stomach and partially in the esophagus. Kenworthy and Welch,[8] Adams and Hoover,[9] and Cornell and his associates[10] have reported finding ulcers which penetrated into leiomyomas. Bryant[11] reported an ulcer associated with a leiomyoma. Adams' case was the only one in which the ulcer did not occur at the lower end of the esophagus.

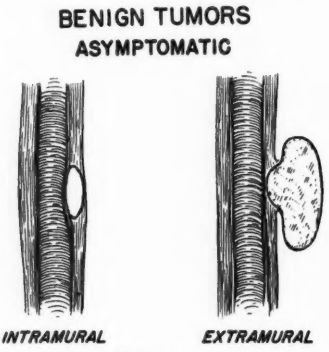


Fig. 1.

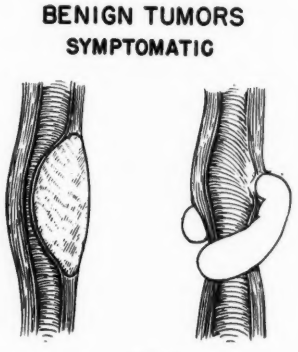


Fig. 2.

Fig. 1.—Diagrammatic sketch of two types of benign muscle wall tumors of the esophagus which rarely cause symptoms.

Fig. 2.—Diagrammatic sketch of two types of benign muscle wall tumors of the esophagus which cause symptoms. The one shown on the left is intramural, submucosal, and compresses the esophageal lumen. The one on the right is extramucosal, but has caused a small traction diverticulum of the mucosa. Its encircling arms have caused some obstruction of the esophagus.

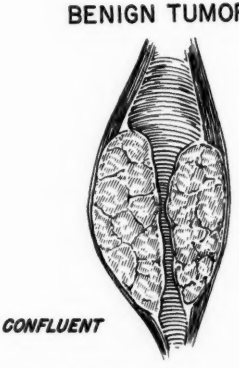


Fig. 3.—Diagrammatic sketch of benign muscle wall tumor of the esophagus appearing in a large confluent submucosal mass causing partial obstruction.

As in the uterus, leiomyomas of the esophagus can be single, multiple, simple, nodular, bosselated, or lobulated. Multiple benign tumors were found among four of our patients. Multiple tumors were found in nine different individuals in the series of cases collected by Rose.[4] Calmenson and Clagett[13] removed two at one operation. Cornell, Lyons, and others[10, 14] have reported

them. Sixteen of our twenty patients had single tumors. Of these, six were nodular, bosselated, or lobulated. Although these types of growth as a rule do not give rise to symptoms different from those of the simple ones, their excision can be much more difficult. The reason is that they often present multiple, adherent projections of tumor among the muscle fibers, so that considerable muscle damage is entailed by their removal. In one of our patients a horseshoe-shaped tumor was found lying outside of the lower end of the esophagus. It caused dysphagia by external constriction. A similar encircling tumor arising at the same level and causing dilatation of the esophagus was reported by Eberth in 1868.[15] Two more are listed by Rose.[4]

Size is the most important single factor in the production of symptoms by these growths. Although Oshawa[16] excised a myoma only 1 cm. in diameter because it caused symptoms, the smallest of our twelve symptomatic growths measured 3 cm. in diameter. Most of our tumors treated surgically were over 5 cm. in diameter. Most of the surgically treated tumors reported in the literature have been at least 3 cm. in diameter. Three of our tumors occupied the entire lower third of the esophagus. Harrington[17] resected a similar tumor. The largest of ours weighed 675 grams. Schnug[7] removed one weighing 632 grams. Other large tumors have been reported.[4] Large tumors do not always cause symptoms. This is particularly true of those which lie outside of the esophageal wall and are connected to it only by a pedicle which extends through to the submucosa. Two such tumors in our series, measuring, respectively, 4 and 5 cm. in diameter, were found at autopsy. No evidence of symptoms related to their presence could be found in the patients' histories. These extramural tumors, if they lie freely in the mediastinum or abdominal cavities and neither press on surrounding organs nor pull on the esophagus, can be completely asymptomatic. Miller found such a one measuring 6 inches in length at the autopsy of a young man.[18] It lay in the abdominal cavity. Daniel and Williams[19] removed a leiomyoma, which measured 13 cm. in its greatest diameter, from the mediastinum of a woman who had no complaints. Other extramural tumors have caused symptoms, however, as did one of ours.[7, 17, 20]

Most of the benign muscle wall tumors remain beneath the muscle. They cause pain, dysphagia, and digestive symptoms as they grow larger because of the pressure they exert on the muscularis and the esophageal lumen. As they become larger, they tend to encircle the lumen. The muscularis over them gradually thins into a tense, hard, densely adherent sheath from which it is often impossible to dissect the tumor free. This led to esophageal resection in two of our cases and one reported by Chi and Adams.[21]

Diverticula have been found associated with benign tumors in a number of instances. Four have been reported as occurring in autopsy specimens.[4, 22] One in our series was found in conjunction with an extramural tumor. Three other surgeons have noted the presence of diverticula associated with surgically treated leiomyomas.[7, 17, 20] The possibility that the weight of an extramural tumor could exert a traction effect through the attachment of its pedicle was suggested by Hoyne and Rogers.[20] Certainly, an extramural tumor of

sufficient size, unsupported by surrounding structures, would draw the muscularis outward and downward at the site of its attachment, creating a mucosal pocket. This was apparently the mechanism involved in our case.

*2. Sarcomas.*—Considerable difference of opinion exists among pathologists as to the classification of sarcomas of the esophagus. The German pathologists[2, 3] have divided them into two main groups: polypoid lesions and diffuse, infiltrating ones. The only true muscle wall sarcomas are the leiomyosarcomas, fibrosarcomas, and rhabdomyosarcomas. These exist usually in the form of rough, polypoid tumors. Their identification depends on the use of smooth muscle stains. Our two specimens were carefully studied and fresh slides were made. The previous diagnosis of leiomyosarcoma and rhabdomyosarcoma, respectively, were confirmed. The leiomyosarcoma, which has already been reported,[12] was a diffuse, infiltrating lesion occupying a third of the esophagus. It was ulcerated and had metastasized to the regional lymph nodes. The rhabdomyosarcoma was a polypoid growth 6.5 by 4 by 2.5 cm. in size, attached to the muscle wall by a stalk 6.5 cm. long and 0.5 cm. in diameter. It projected into the lumen and was covered with hemorrhagic tissue. It had not metastasized.

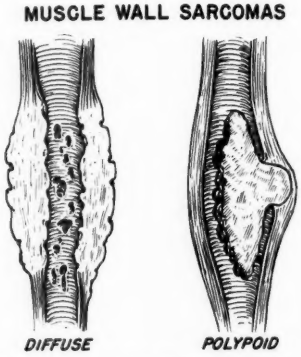


Fig. 4.—Diagrammatic sketch of the two major types of muscle wall sarcomas of the esophagus. That on the left is diffuse and infiltrating with a rough surface. That on the right is a localized irregular polyp.

Although sarcomas arising in the mucosa and submucosa of the digestive tract are usually rapidly growing and highly malignant, leiomyosarcomas are characterized by slow growth, long duration of symptoms, and a low incidence of local and distant metastases.[23] The time from onset of symptoms to death in our case was twelve years, which gives rise to the conjecture that the original tumor might have been benign.

The literature is very scanty regarding malignant esophageal muscle wall tumors. A number of the tumors described in the literature are diagnosed in terms which leave much doubt as to their true histology. Little is to be gained, therefore, in discussing them. Three leiomyosarcomas have been successfully resected.[1, 14, 24] Two were polypoid and one was a nodular diffuse tumor. In two cases there was no evidence of metastases; in the other, no statement was made concerning them. Thorek's[2] rhabdomyosarcoma, like

our own, was polypoid and had not spread. The fibrosarcoma removed by Clark[25] was polypoid and showed no metastases. That removed by Brea[26] was submucosal, well circumscribed, and indistinguishable from a leiomyoma roentgenographically. The polypoid tumors tend to become necrotic and to bleed. Clark's tumor apparently broke off and was swallowed early in its course and then grew out again. Garlock's[14] tumor broke free from its slender pedicle at the time of operation.

### INCIDENCE AND SITE OF ORIGIN

Although many benign esophageal tumors have been reported in the literature, we have no studies that might reveal the true incidence of benign muscle wall tumors. Autopsy findings are inconsistent and inadequate. Thirty-three of these tumors were found in 7,459 autopsies at the Mayo Clinic.[27] Eleven benign growths were reported from 6,301 autopsies at the University of Chicago clinics.[28] No leiomyomas were found in 4,000 autopsies at the Vanderbilt University Hospital.[19] Only four muscle wall tumors were found in 13,000 autopsies at the Massachusetts General Hospital. At the same time there were four instances in which these tumors were discovered in conjunction with, but quite separate from, carcinomas in a few hundred surgically resected esophaguses. Pathologists when performing autopsies are not likely to make a detailed search for neoplasms in apparently normal organs. Meissner, at a time when leiomyoma of the stomach was believed to be rare, carried out extremely careful examinations of fifty post-mortem stomachs selected at random. He found leiomyomas in forty-six out of fifty stomachs so studied.[29] There is no reason to believe that these lesions exist in the esophagus with similar profusion, but certainly we would have a better idea as to their occurrence if someone were to carry out studies by Meissner's technique in a few hundred autopsy specimens.

Esophageal muscle wall sarcomas are extremely rare. Because the histologic diagnosis is uncertain in all but the most recent literature, we have only a very small amount of material upon which we can base any figures. In general their occurrence in this organ is less frequent than in the remainder of the digestive tract. Corner and Fairbank[30] found that among 175 sarcomas of all kinds in the alimentary canal, only 8 per cent had arisen in the esophagus. In the past twenty years, forty-six patients have been operated upon for removal of benign muscle wall neoplasms of the esophagus. In the same period we have reports of seven muscle wall sarcomas which were resected and five more which were not. Sarcomas as contrasted with benign tumors usually produce symptoms and are seldom so insignificant as to be overlooked at autopsy.

Among the twenty patients in our series who had benign tumors, the growths were found in the lower esophagus in thirteen instances, in the middle in five, and in the upper third in two. The fact that the distribution is similar to those previously reported serves to indicate that these tumors may occur anywhere but do so predominantly in the lower esophagus.

Sarcomas of all types are found most frequently in the lower portion of the esophagus.[2, 3] The leiomyosarcoma in our series occupied the entire lower

third. The rhabdomyosarcoma, which has been previously reported, occurred just below the aortic arch.[31] Of the tumors reported recently, about which the pathologic diagnosis is reasonably certain so that they are subject to classification, Harrington's leiomyosarcoma lay in the lower third, as did a second inoperable tumor in his series.[24] Resano and Hojman's[1] leiomyosarcoma lay in the cervical esophagus as did that of Menne and Birge.[33] Garlock's[14] lay in the middle third, that of Pennes and the one reported by French and Garland[34, 35] in the same area. Clark's[25] fibrosarcoma grew in the upper esophagus, Brea's[26] was found in the lower third. Dvorak's[3] rhabdomyosarcoma was found in the upper third, Thorek's[2] lay just below the arch of the aorta.

### AGE AND SEX

The four benign tumors in our series found at autopsy were apparently asymptomatic. Two were in men, two in women, the ages being 30, 49, 64, and 72 years, respectively. From our knowledge of uterine fibroids it may be assumed that these tumors can exist without evidence of growth for many years. It is therefore impossible to say whether these tumors were of recent origin or whether they had existed in a quiescent state for a large portion of the patient's life. Of the four found coexistent with carcinoma, three were in men and one in a woman; the ages of the patients were 56, 63, 65, and 67 years, respectively.

Of the twelve patients who had symptomatic benign tumors, seven were men and five women. The youngest was 19 years, the oldest 67 years; the average age was 41.2 years. The length of time which these patients had noted symptoms, however, was from three months to twelve years, with an average of a little over four years. The average age at onset of symptoms was 37.1 years. Myers and Bradshaw,[5] in 1951, made a survey of some twenty-nine cases of benign muscle wall tumors of the esophagus treated by surgery (excluding Churchill's case, which is included in our series). Seven more have appeared in the literature, including one of theirs. The age range of this group of thirty-six patients was from 14 to 66 years, with an average age of 41.6 years. The ages of the patients at the time of surgery in our series are very similar to those previously reported. The average age is lower than that ot patients suffering from malignant neoplasms of the esophagus (Table I).

TABLE I. BENIGN TUMORS. AGE AT TIME OF SURGERY OF 47 SURGICALLY TREATED PATIENTS

| | THIS SERIES 11 CASES | PREVIOUSLY REPORTED 36 CASES |
|---|---|---|
| Minimum | 19 | 14 |
| Maximum | 67 | 66 |
| Average | 41.2 | 41.7 |

The sex division among the patients reported in the literature is 19 men and 17 women (Table II). Our own series of eleven patients treated surgically was comprised of six men and five women. This makes a total of forty-seven patients, if our series is added to the literature, twenty-five of whom were men

TABLE II. BENIGN TUMORS. SEX OF SURGICALLY TREATED PATIENTS

| | THIS SERIES | PREVIOUSLY REPORTED | TOTAL |
|---|---|---|---|
| Men | 6 | 19 | 25 |
| Women | 5 | 17 | 22 |
| Total | 11 | 36 | 47 |

and twenty-two of whom were women. Judging by this small group of cases there seems to be little difference in the sex incidence of benign muscle wall tumors.

Although the average age of patients with sarcomas of all types of esophageal origin has been reported to be the same as that of carcinoma,[3] the average age of the seven patients who have had malignant muscle wall tumors removed surgically (including our own) was 56.7 years, with a range of 43 to 78 years. Dvorak's[3] patient with a leiomyosarcoma was only 27 at the time of death and the tumor could have been removed surgically had modern techniques been available. For esophageal sarcoma in general, the incidence among men as compared with women is three to one. Among the patients with malignant muscle wall tumors diagnosed in recent years, of which the histologic classification is reasonably certain and the sex has been recorded (including our own cases), there have been seven men and four women.

The rhabdomyosarcoma in our series occurred in a woman 78 years old, who had had symptoms for four months. The leiomyosarcoma occurred in a man of 61 who had had symptoms for twelve years.

## SYMPTOMATOLOGY

*1. Benign Tumors.*—Among our patients and those whose symptoms have been described in the literature, there is no consistent common symptomatology of benign esophageal wall tumors. There are, however, three general classes into which the symptoms which have been noted may be said to fall. These are *pain, dysphagia,* and *digestive symptoms.* In considering the benign lesions we confined our study to the tumors diagnosed surgically, twelve in number, eleven of which were operated upon (Table III). The tumors found at autopsy had apparently caused no symptoms. The four found in conjunction with carcinomas could not be properly evaluated.

*Pain* was a prominent symptom among nine out of twelve of our patients. It was of the type ordinarily associated with lesions of the esophagus. It was either substernal or epigastric, and usually it radiated. The areas of radiation varied considerably but included the back, scapula, shoulder, neck, or even down either arm. Deglutition seldom produced pain immediately, but in most instances the pain was related in some way to eating although not directly with the act of swallowing. In four of these patients the discomfort bore so little association to meals that they were suspected of having cardiac disease, for which three were actually treated. It should be noted that two of these patients and one other, who had pain but was not suspected of having a cardiac disorder, had hiatus hernias in addition to their tumors. Seven of these patients had pain of sufficient severity to warrant the statement that it was their chief complaint.

TABLE III. BENIGN TUMORS. COMPARISON OF CHIEF COMPLAINTS OF PATIENTS TREATED SURGICALLY*

| | OUR SERIES | REPORTED CASES | TOTAL |
|---|---|---|---|
| Pain | 6 | 8 | 14 |
| Pain and dysphagia | 1 | 5 | 6 |
| Dysphagia | 3 | 6 | 9 |
| Digestive symptoms | 1 | 9 | 10 |
| Other (Mostly respiratory) | | 4 | 4 |
| None | | 4 | 4 |
| Total | 11 | 36 | 47 |

*This table includes both our series and cases of benign muscle wall tumors of the eosphagus reported in the literature. Most of these patients had several complaints.

*Dysphagia* was found among ten of these patients. Their complaints varied from a rare one of food sticking occasionally to a constant inability to swallow solid food. There was no evidence of even temporary complete obstruction among any of these patients. Only two required a consistently modified diet. Six, however, by giving a history of weight loss, presented concrete evidence that obstruction had interfered with their alimentation. This weight loss varied from ten to twenty-eight pounds and averaged fourteen pounds. Three of these patients presented dysphagia as a chief complaint. In addition another had experienced an almost exsanguinating hemorrhage immediately prior to his hospital entry.

*Digestive Symptoms* were interesting because it is difficult to correlate them with esophageal lesions. They were characterized by gas, eructations, heartburn, nausea, vomiting, or postprandial distress. These symptoms were presented by five patients. Two others, who gave a history of ulcer proved by pathologic examination of the stomach or by roentgenogram, had similar symptoms but are not included. These digestive complaints were prominent ones as given by these patients, but in only one did they form the basis of his chief complaint. This particular patient also complained of occasional dysphagia. The tumor lay behind the arch of the aorta. He obtained good symptomatic relief from surgery.

In summary, the chief complaint was esophageal pain in seven patients, dysphagia in three, digestive symptoms in one, and massive hemorrhage in one. Only three patients had complaints falling into all three of the major groups of symptoms.

The length of time which these symptoms had been present was on the whole consistent with what one would expect of benign lesions. The shortest history of symptoms was three months, the longest twelve years, the average four and one-half years. The complaints were seldom constant or of gradually increasing intensity, but were usually intermittent and of variable severity.

Reviewing histories reported in the literature is not as revealing as talking to patients or studying a detailed hospital record, insofar as the interpretation of symptoms is concerned. A rough idea as to the symptomatology of these benign tumors can be obtained, however, by listing the chief complaints of the patients. These are presented in Table III. Briefly, pain alone was the chief complaint among eight of the thirty-six patients so far reported,

pain and dysphagia together were found in another five, dysphagia alone in six more, digestive complaints in nine, other complaints (mostly of a respiratory nature) in four, and no symptoms at all were found among the remaining four patients. Dr. Churchill's patient is included in our series and not among those reported previously.

*2. Muscle Wall Sarcomas.*—In general the symptomatology of the esophageal sarcomas closely parallels that of the squamous-cell carcinomas. There are, however, some distinguishing differences, as other writers have previously remarked.[2, 3, 14] The first of these differences is that pain, which is rarely presented as a symptom of carcinoma, is a conspicuous complaint among patients suffering from muscle wall sarcomas. Our patient who had a rhabdomyosarcoma had considerable pain. Seven other authors have described this finding.[1-4, 24, 33, 35] The leiomyosarcoma in our series, one of those reported by Harrington,[24] and the fibrosarcoma described by Clark[25] are conspicuous exceptions to this rule as they apparently caused no pain.

Marked weight loss, inconsistent with the degree of esophageal obstruction, is another outstanding symptom of muscle wall sarcoma. Our patient with the leiomyosarcoma lost fifty pounds; the other patient lost twenty, yet both patients were capable of swallowing sufficient amounts of nourishing fluids to maintain their weight. Clark's patient had lost thirty pounds, Garlock's forty, and Dvorak's forty, yet none of these patients had sufficient obstruction to prevent an adequate intake.

Dysphagia is the principal symptom of all patients suffering from sarcomas, but in the cases of muscle wall sarcoma it rarely reaches the degree associated with the stenosing carcinomas. Regurgitation of foul mucus was a prominent complaint of our patient whose leiomyosarcoma had ulcerated. Regurgitation and salivation have been reported as symptoms previously.[1, 2, 24] As these tumors often become necrotic and bleed, both anemia and tarry stools have been found associated with them.[3]

## DIAGNOSIS

*1. Benign Tumors.*—It is obvious from the multifarious symptoms associated with benign tumors of the esophageal muscularis that the patient's history is of little help to the surgeon in making a diagnosis. Neither is a physical examination. If the tumor is confined by the muscle wall and protrudes with a smooth unbroken curve into the lumen, a roentgenogram after a swallow of barium may give a picture typical of a benign tumor.[32] As the barium passes evenly over the lesion into the normal esophagus below, it becomes apparent that the mucosa is intact. The unroughened continuity of the mucosa in the region of the growth demonstrated by such means helps to distinguish the extramucosal lesions from destructive growths involving the epithelial layer. Smooth indentations in the tumor mass are indicative of bosselation, lobulation, or multiple growths.

The difficulty of interpreting such findings has been pointed out by Schatzki and Hawes[38] who demonstrated similar defects produced by lymph

nodes, mediastinal structures, and extramural neoplasms. All of the single lesions in our series were identified roentgenographically as extramucosal benign tumors. The presence of ulceration renders diagnosis more difficult.

Small intramural growths, of less than 1 cm. in size, frequently escape the notice of the roentgenologist. Very large tumor masses which angulate the esophageal wall and distort the lumen over a considerable area sometimes remain undiagnosed preoperatively. The huge tumor in our series which gave this appearance had been called "cardiospasm" for years. The appearance of dilatation above an area of constriction in the lower esophagus has led to this confusion before.[16, 39] Our other two large tumor masses were correctly identified by roentgenograms.

Fig. 5.—Lateral and posteroanterior views of roentgenograms of a simple submucosal benign muscle wall tumor of the esophagus after a swallow of barium, showing its smooth outline and projection into the lumen.

Extramural growths without sufficient attachment to the muscle wall to cause distortion usually defy identification as esophageal tumors. Those masses which are accompanied by traction diverticula, however, should be suspected of being muscle wall tumors.

Esophagoscopy has been frequently employed in the study of these lesions. If the esophagoscope can be passed down to and past the lesion so that the endoscopist can be reasonably certain that he has viewed an entirely intact mucosa, he can assure the surgeon that the tumor is not a carcinoma. It is impossible, however, by this means to identify positively either the various types of benign tumor or noninvasive sarcoma of the muscle wall.

Endoscopic biopsy of these lesions through an intact mucosa is seldom fruitful, potentially dangerous, and renders subsequent enucleation without contamination impossible. Five of our patients who had symptomatic tumors

were esophagoscoped. Biopsies were obtained in four. One of these showed a leiomyoma; two produced no abnormal tissue. One was incorrectly diagnosed as a carcinoma.

In a number of instances reported in the literature esophagoscopy without biopsy was helpful in confirming the presence of an apparently benign extra-

Fig. 6.—Roentgenogram of a large mass of submucosal confluent leiomyomas showing angulation of the esophagus.

Fig. 7.—Simple leiomyoma enucleated from the esophageal wall because it had caused dysphagia.

mucosal lesion.[9, 10, 17, 40] Biopsy has failed to obtain tumor in some cases because of the thickness of the overlying esophageal wall.[39, 41, 42]

Benign muscle wall tumors should be kept in mind as a diagnostic possibility in patients of all ages and both sexes who have epigastric or chest pain, dysphagia, or digestive symptoms. If careful roentgenographic studies are made, the diagnosis will often be apparent. Observation esophagoscopy is helpful in ruling out tumors which involve the mucosa.

*2. Sarcomas.*—The diagnosis of muscle wall sarcoma of the esophagus has not always been made prior to surgical resection or autopsy in the past. The presence of a muscle wall sarcoma should be suspected in a patient thought to have a carcinoma when pain accompanying deglutition is a prominent symptom, when weight loss and cachexia are disproportionate to the degree of obstruction, and when a roentgenogram demonstrates a polypoid tumor. This is particularly true if the symptoms are of long-standing. The leiomyosarcoma in our series was undiagnosed until the tumor was studied microscopically after autopsy. The rhabdomyosarcoma was identified after resection.

Biopsy through the esophagoscope is the best means of establishing the diagnosis preoperatively. The first successful identification of a sarcoma by this means was made by von Hacker in 1903.[43] Among the cases reported in the recent literature at least six such successful biopsies are recorded.[1-3, 14, 24, 25] In four more including one of our own, biopsy specimens were wrongly diagnosed as carcinomas.[2, 33, 35] The reason for failure has been the presence of hemorrhagic necrotic tissue covering the tumor. In order for the biopsy specimens to be adequate for pathologic identification, they should be large and deep.

## THERAPEUTIC CONSIDERATIONS

*1. Benign Tumors.*—Most of the benign muscle wall tumors reported so far have been asymptomatic. Four of ours found at autopsy certainly were so and the four found in esophageal segments resected for carcinoma apparently caused no trouble. All of these tumors were either small or extramural. Although these asymptomatic lesions may not grow for years and appear to be harmless, their positive identification as benign can be established only by biopsy or excision. It has been necessary occasionally to remove such tumors in order to determine their exact nature when they were roentgenographically indistinguishable from malignant neoplasms of the mediastinum.

Small tumors causing symptoms should be removed as soon as possible to avoid the surgical difficulties incurred by their becoming so intimately adherent to the esophageal wall or of growing to such a size that they can be removed only by esophageal resection.

Simple enucleation without entering the mucosa, followed by reconstruction of the esophageal wall, is the treatment of choice. This procedure was carried out on seven of our patients, one of whom died postoperatively of anesthesia complications. Nineteen tumors reported by Myers and Bradshaw[5] were removed in a similar fashion, excluding Dr. Churchill's case.

One of these patients died postoperatively. Since their summary was written, four more tumors have been reported as successfully enucleated by Engelking,[40] Tuttle,[44] Guetgemann,[42] and Myers and Bradshaw.[5]

Two of our patients had tumors which were excised along with small segments of mucosa. They both made uneventful recoveries. Two similar successful cases are listed in Myers and Bradshaw's summary.[5] Westerborn[39] has since reported another.

Fig. 8.

Fig. 9.

Fig. 8.—External appearance of a surgically resected specimen of the lower esophagus and stomach containing multiple confluent leiomyomas.

Fig. 9.—The intraluminal appearance of the specimen shown in Fig. 8.

In our cases, three of the tumors were approached from the right side of the chest and six from the left. If the tumor preoperatively appears to be simple and not so large or extensive that the muscle coat over it cannot be preserved, the approach can be made as a matter of operative convenience depending upon the position and projection of the tumor. If doubt exists as to the possibility of local excision, however, because of the size or the extent of the lesion, the surgeon should prepare preoperatively for esophageal resection. In one case reported in the literature enucleation was impossible when

the tumor was approached from the right and a second operation was necessary on the left in order that the esophagus could be resected.[21] In another case the attempted enucleation of an extensive tumor ended in failure.[45]

Two of our patients required resections of the esophagus in order to remove the tumor mass. In one of these the diagnosis was established preoperatively by roentgenogram and a resection was planned preoperatively. The other patient had been treated unsuccesfully for esophagitis and what was termed "cardiospasm" in a number of clinics for nine years. He entered the hospital after an exsanguinating hemorrhage. Previous films had shown evidence of esophageal ulcer. After multiple blood transfusions he was operated upon as an emergency with the true diagnosis unsuspected. The tumor was identified at operation and the esophagus and part of the stomach into which the tumor had intussuscepted were resected. Both of these patients made satisfactory recoveries. Seven resections for benign tumors, with two deaths, have been reviewed by Myers and Bradshaw.[5] Schnug has also reported a successful resection[7] (Table IV).

TABLE IV. SURGICAL TREATMENT. TYPES OF OPERATIVE APPROACH TO BENIGN MUSCLE WALL TUMORS

| | THIS SERIES | | PREVIOUSLY REPORTED | | TOTAL | |
|---|---|---|---|---|---|---|
| | NO. OF CASES | OPERATIVE MORTALITY | NO. OF CASES | OPERATIVE MORTALITY | NO. OF CASES | OPERATIVE MORTALITY |
| Enucleation | 7 | 1 | 22 | 1 | 29 | 2 |
| Attempted enucleation | 0 | 0 | 1 | 1 | 1 | 1 |
| Excision with mucosa | 2 | 0 | 4 | 0 | 6 | 0 |
| Resection | 2 | 0 | 9 | 2 | 11 | 2 |
| Total | 11 | 1 | 36 | 4 | 47 | 5 |

The technique of esophageal resection is now so well standardized as to require no comment here other than to state that the large resection margins required in cancer surgery are unnecessary in handling benign tumors. Local excision is of more interest. An esophagus which contains a large intramural benign tumor has the appearance of being engorged with a tumor mass. The appearance is somewhat analogous to that of a boa constrictor which has recently swallowed a pig. If the esophagus is freed up, it can be drawn out of the mediastinum so that the area in which the tumor projects may be identified by rotating the esophagus with the hand. A longitudinal incision made over the presenting area of the tumor followed by gentle pressure by the surgeon's hand as it encompasses the esophagus will usually cause the tumor to extrude from the muscularis. If the tumor is adherent to the mucosa or muscle fibers, it can be gently dissected free. If necessary, a small portion of mucous membrane can be excised with it. Care must be exercised to remove the intramuscular pedicle of extramural tumors to avoid the possibility of recurrence. The technique of closure of the esophageal wall has been too well described many times before to warrant comment here.

One of our patients with a huge mass of confluent leiomyomas surgically diagnosed by biopsy through an esophagoscope has not yet had a resection. He did not desire surgery, nor was it deemed advisable once the tumor was determined to be benign. His pain and dysphagia were both intermittent and

moderate. His chief difficulty consisted in duodenal obstruction from an active duodenal ulcer which had been present for twenty-five years. The ulcer required immediate treatment which was provided in the form of a transabdominal vagectomy and pyloroplasty. This combination of procedures was elected in order to preserve the full length of the stomach should his esophageal tumor ultimately require resection. In the five years which have passed since this operation, his dysphagia and esophageal pain have not changed. Roentgenographically the leiomyomas have not become more extensive but show signs of increasing calcification. Malignant degeneration has not become evident.

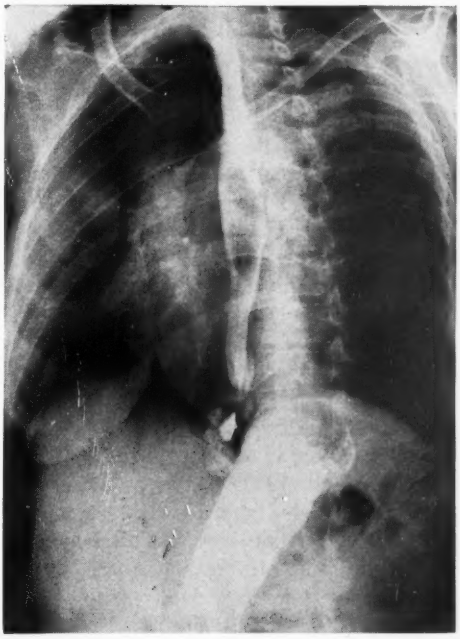

Fig. 10.—Roentgenogram of a partially calcified extramural leiomyoma which encircles and partially occludes the esophagus. A small barium-filled esophageal diverticulum lies over the tumor on the left.

Among the forty-seven patients (including eleven of our own) whose benign esophageal wall tumors were treated surgically, the results are as follows: In one patient the tumor could not be removed.[45] She died postoperatively. In another some tumor was left behind.[17] The remaining forty-five patients reportedly had complete removal of their growths. Four of these patients died postoperatively. Four of the remaining forty-one had no symptoms preoperatively. The remaining thirty-seven patients apparently obtained good symptomatic relief from surgery.

*2. Sarcomas.*—Both radiation therapy and surgery have been employed in the treatment of the muscle wall sarcomas. As might be expected in dealing with tumors of muscular origin, radiation therapy has not been successful.

The diagnosis in the cases so treated was established by pathologic means as rhabdomyosarcoma[3] in one case and leiomyosarcoma[33, 34] in two, and fibrosarcoma in a fourth.[26]

In reviewing the muscle wall sarcomas treated surgically we have confined our studies to those tumors of which the histologic identification was sufficiently clear so that there could be little question as to the classification of the tumor both as to its site of origin or its cell type. Most of the cases reported in the foreign literature, particularly in articles written more than twenty years ago, despite detailed histologic descriptions, defy identification in terms of our present-day nomenclature. To draw conclusions as to clinical behavior of tumors of which the exact diagnosis is in doubt is misleading. Although the treatment of these unidentifiable sarcomas is not statistically important, it is of considerable historical interest. At the end of the last century and early in this one gastrostomy was frequently performed to combat starvation secondary to dysphagia and obstruction. Tracheotomy was sometimes employed to prevent asphyxia if the lesions involved the pharynx.

Direct attack was first carried out upon cervical sarcomas because of their accessibility. In 1875 Baum[46] excised locally a polypoid sarcoma of the pharynx which extended into the esophagus.[46] Von Hacker[43] resected a muscle wall tumor of the cervical esophagus in 1903. The patient died of pneumonia and metastases three months later. The pathologic description of this tumor we have had translated into English and reviewed by a pathologist who thought that the tumor was probably a fibrosarcoma but could not be certain.[47] Snoy[48] successfully removed a sarcoma of the esophagus and pharynx in 1911.

Because of their inaccessibility, the sarcomas of the thoracic esophagus remained inviolate until Harrington successfully resected a diffuse leiomyosarcoma of the lower third in June, 1945.[24] The rhabdomyosarcoma in our series was resected in July, 1945, and a supra-aortic esophagogastric anastomosis was performed. The patient was an emphysematous, malnourished woman 78 years old with severe arteriosclerotic heart disease. She died of pulmonary infection and cardiac failure on the twentieth postoperative day. No metastases were found either at operation or at autopsy.

Garlock[14] resected a leiomyosarcoma in 1946. The patient was well six years later. Clark[25] successfully resected a fibrosarcoma in 1947. Thorek[2] was able to carry out a successful resection of a rhabdomyosarcoma in 1948. Brea[26] reported enucleating a well-circumscribed extramucosal tumor of the lower esophagus in 1948. Although the tumor was believed preoperatively to be a leiomyoma, pathologic section proved it to be a fibrosarcoma. The tumor recurred two and one-half years later, was resistant to radiotherapy, and the patient subsequently died. Resano and Hojman[1] successfully resected a leiomyosarcoma of the cervical esophagus by the Wookey technique in 1951. These cases are outlined in Table V.

Considering the good early results obtained in this small group of cases, surgical resection is the treatment of choice for both diffuse and polypoid muscle wall sarcomas. Palliative resection of carcinoma of the esophagus is

TABLE V. SARCOMAS OF THE ESOPHAGEAL MUSCLE WALL REMOVED SURGICALLY

| SURGEON | YEAR | AGE | CHIEF COMPLAINT | TYPE OF TUMOR | DIAGNOSIS | RESULT |
|---|---|---|---|---|---|---|
| Harrington | 1945 | 60 | Pain, dysphagia | Nodular and diffuse | Leiomyosarcoma | Recovered |
| Sweet | 1945 | 78 | Pain, dysphagia | Polypoid | Rhabdomyosarcoma, no metastases | Died |
| Garlock | 1946 | 58 | Pain, dysphagia | Polypoid | Leiomyosarcoma, no metastases | Well 6 yr. later |
| Clark | 1947 | 43 | Dysphagia | Polypoid | Fibrosarcoma | Recovered |
| Brea | 1948 | 65 | Dysphagia | Intramural | Fibrosarcoma, no metastases | Recurred 2½ yr. later |
| Thorek | 1948 | 43 | Pain, dysphagia | Polypoid | Rhabdomyosarcoma | Recovered |
| Resano and Hojman | 1951 | 50 | Dysphagia | Diffuse | Leiomyosarcoma, no metastases | Recovered |

of proved value in lengthening the life of the patient and rendering his life more bearable by restoring continuity of the alimentary tract and by relieving pain. Palliative surgery for extensive spindle-cell sarcomas of the esophageal wall would appear to be justifiable on the same grounds. Salivation and regurgitation of foul mucus were distressing symptoms late in the disease of our patient who died of a diffuse ulcerated leiomyosarcoma, as they have been in cases reported by others. The avoidance of these symptoms is an additional reason for advocating palliative resections.

## SUMMARY AND CONCLUSIONS

A series of twenty-two muscle wall tumors of the esophagus has been presented. Twelve of these, one malignant and eleven benign, were removed surgically. A correlation has been made between those previously reported and our observations of the pathologic and clinical manifestations of these growths, their diagnostic characteristics, their treatment, and the results of therapy.

The benign tumors, although distinguishable from one another by careful histologic study, are so closely related in terms of clinical behavior that they may be grouped together. Most small benign tumors are usually asymptomatic, but when they become larger than 1 or 2 cm. in diameter, they may cause symptoms if they remain intramural. Extramural tumors can be confused with malignant tumors of the mediastinum, but only produce symptoms by encircling the esophagus or by pressure on adjacent viscera. A presumptive diagnosis of a benign tumor can usually be made roentgenographically. Esophagoscopic examination may help to rule out carcinoma, but biopsy is seldom helpful and may be harmful. The best treatment for symptomatic benign tumors is local excision, but esophageal resection may be necessary if the tumors are large, extensive, or multiple. The mortality of the surgical treatment of benign lesions should be low. The results of such treatment are good.

The primary sarcomas are extremely rare and little is known about them. The experience with surgical removal of sarcoma is small. The diagnosis of these tumors preoperatively depends upon an adequate biopsy. The ideal

treatment of muscle wall sarcoma is resection. There is some promise that polypoid sarcomas arising in the muscularis can be cured in a high percentage of cases, as they are slow growing and slow metastasizing.

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## DISCUSSION

DR. RICHARD H. MEADE, Grand Rapids.—This has been a beautiful presentation and my object in arising is not to discuss the total subject. In 1946 Dr. Kay reported on the benign tumors of the esophagus from Kennedy General Hospital. So far as I know, those cases have never been reported by others in speaking of benign tumors. Of the two cases we had, both were extramucosal tumors; the first was at the lower end of the esophagus and was readily enucleated without difficulty. The second one involved the upper esophagus and also was enucleated without difficulty, so we thought, but the patient later developed aseptic necrosis of the esophagus and died. We were not aware at the time of operation that the blood supply was interfered with. I should like to ask Dr. Soutter and Dr. Sweet if tumors in this particular region should be handled in a different way.

DR. JOHN F. HIGGINSON, Portland.—I enjoyed the presentation of Dr. Soutter and Dr. Sweet. The question of what to do with the benign variety of these smooth muscle tumors is a difficult one to decide, particularly if the case is further complicated by a multiplicity of tumors, and aside from the question of malignancy which is, of course, always present. I would like to use a case to demonstrate this particular feature.

(Slide.) This is the preoperative roentgenogram of a barium swallow in a 30-year-old man, whose condition was noticed after a routine chest survey x-ray examination showed a large mediastinal tumor in the lower chest, which apparently involved the esophagus. This picture demonstrates the large tumor of the lower esophagus with obvious distortion of the esophagus, and also shows several other tumors above. Esophagoscopy was done on two occasions and, as the authors stated, both esophagoscopic examinations were unhelpful. At 29 and 35 cm. from the upper incisor teeth there were small irregularities in the esophageal mucosa which, however, did not yield any particular information. There was, of course, lower in the esophagus the deformity one would expect from such a tumor as this large one.

(Slide.) This gives a rough idea of the general size of the tumor; because this tumor was so large and involved a good portion of the lower esophagus and because there was also a multiplicity of tumors (we were able to palpate the two other tumors in the middle and upper esophagus), we did not feel that we should resect the esophagus in this 30-year-old man who had no symptoms except occasional gagging when he swallowed. Moreover, the tumor extended out of the esophagus down into the cardia and fundus of the stomach, and it would have required a proximal gastric resection and a distal esophageal resection in order to remove it by resection.

(Slide.) Accordingly, the tumor was removed by the method described by the authors, and it was rather surprising to find that by tedious dissection it was possible to remove this tumor from within the interstices of the splayed-out fibers of the esophagus. The only portion of the esophageal wall which was at all still present as true wall was the right aspect of it, and this retained sufficient circulation to permit repair of the esophagus. This tumor was 7 by 17 cm., with the tonguelike extension seen here going down to the stomach, measuring 4 by 15 cm. The total weight was 645 Gm. It was an obvious, usual, typical leiomyoma.

(Slide.) This is a postoperative roentgenogram showing the normal-looking lower esophagus, although you will note there seems to be an esophageal hiatal hernia. There was indeed a small one at operation which was repaired. This is not a hernia, the radiologist tells us; it is merely the broadened and still rather large lumen of the esophagus which had been originally distorted in a fishtail manner, and then diminished in caliber by the surgery. We have not as yet taken out the tumors above, and we are letting a considerable period of time elapse until the circulation has returned below, so that when we bother these we will presumably not injure the esophagus irreparably.

DR. JOHN H. GARLOCK, New York.—We would like to report and put on record for the first time seven cases of leiomyoma from our clinic. Three were found incidentally in excised specimens resected for carcinoma. Four were operated upon. I might say that esophagoscopy preoperatively is of considerable help to the surgeon in arriving at a positive preoperative diagnosis, because the esophagoscopist can tell whether there is intact mucosa over the tumor. Under such circumstances biopsy is not advisable. Three of the four were diagnosed preoperatively on the basis of the x-ray findings and esophagoscopy. Three of these were at the lower end; one was in the middle third. Two of those in the lower end were extensive, almost completely encircling the esophagus and having many ramifications in the musculature. It was felt in each instance that in order to effect complete removal and have an intact esophageal lumen, resection would be necessary and this was done. One of those at the lower end was excised by enucleation, as was also the one in the middle third. All the patients recovered and have remained well.

The one case of leiomyosarcoma which was mentioned by Dr. Soutter brings up a point in technique of the operation. This was a very large tumor, measuring 4 or 5 inches in length; it filled the lumen of the esophagus and felt like a large sausage. It was obviously pedunculated. During the process of mobilization of the esophagus the tumor suddenly disappeared. This was quite disconcerting because we did not know where it went. When we incised the diaphragm to mobilize the stomach we found it near the pylorus. The temptation was very great to remove it through a gastrostomy incision and terminate the operation, especially since nothing was palpable in the esophagus at what we thought might be the site of the pedicle. But we went ahead with resection anyway and it was a good thing we did, because there was infiltration of the wall of the esophagus at the site of the pedicle which extended into the muscularis. The tumor proved to be one of high degree of malignancy. If we had not done that, I am sure this patient would not have survived for seven years.

DR. WILLIAM L. WATSON, New York.—In discussing this presentation of rare esophageal sarcomas by Dr. Sweet and Dr. Soutter, of course anything we say must be considered additive and of value only from that viewpoint. But because malignant sarcomas of the esophagus are so unusual I thought it might be of interest to report our ex-

perience. We have one fibrosarcoma of the esophagus that developed twenty years after radiation of the upper neck over a long period of time for a supposedly benign tumor of the thyroid gland. This patient is of interest to us because she had a carcinoma of the breast treated by radical mastectomy; also a carcinoma of the skin developing in the radiated area, and at operation the supposedly benign tumor of the thyroid, which was removed in doing surgery on the cervical esophagus, proved to be a cancer of the thyroid, and the tumor removed from the esophagus was a fibrosarcoma. So this woman is the only patient in our series who has had four cancers—each one arising in a different anatomic structure.

The important group, however, is that comprising the four patients with myosarcoma. Those tumors were located as follows: one at the thoracic inlet, one at the middle third, and two in the lower third of the esophagus. One patient had a local excision and has been well for seven years; two had resections and gastroesophageal anastomoses and are dead, one of local recurrence in four months and metastasis to the liver, and another of disease four and one-half years after surgery. The fourth patient treated by exploration (excisional surgery was not done) and gastrostomy plus x-ray therapy is now alive and has been well for five years.

I should like to show a slide of a patient about whom there may be some controversy. This is the summary of our cases of cancer of the esophagus. In a series of 1,113 there were four leiomyosarcomas, one fibrosarcoma, and one leiomyoma.

(Slide.) This patient's tumor was the first to be discovered on routine barium swallow carried out on all patients without symptoms who were beyond the age of 40 years. She was slightly overweight but otherwise normal. I did an esophagoscopy and did not find any evidence of ulceration and thought we were dealing with a benign muscle wall tumor, so no biopsy was taken.

(Slide.) At operation the tumor, measuring 7 cm. in diameter, was easily excised. It felt like a benign tumor and I considered it to be so; I took out a small amount of the esophageal wall and was able to do a primary closure. Four days later I was informed by our pathologist that this was a malignant tumor.

So we have two points to make. One is that the pathology varies considerably, and the other is that the pathologist may now look back and say that our one case which has gone seven years without recurrence after local excision must therefore be benign. X-ray therapy seems to have something to offer and one patient so treated is alive five years after treatment.

DR. HERMAN MOERSCH, Rochester, Minn.—Dr. Soutter and Dr. Sweet have again presented us with an excellent and instructive paper. I should like briefly to discuss the tumors that they have classified as leiomyoma and leiomyosarcoma and try to emphasize some of the more salient points concerning these tumors. My remarks are based on a recent review which one of my associates, Dr. Bruce Johnston, has just completed of all cases of leiomyomas and leiomyosarcomas of the esophagus in which operation was performed and the type of lesion proved microscopically at the Mayo Clinic during the past twenty years.

During that period, twenty-one patients with leiomyoma of the esophagus underwent operation. In seventeen instances, the leiomyoma was limited to the esophagus, and in the four remaining cases the tumor involved the lower end of the esophagus and extended into the cardiac end of the stomach. During the same period, five patients having leiomyosarcoma of the esophagus underwent operation. It is of interest that fifteen of the patients having leiomyomas limited to the esophagus were men and only two were women. The four patients who had leiomyomas which extended into the cardiac end of the stomach were women.

With respect to the symptoms of leiomyoma of the esophagus, our experience was similar to that of the essayists. In seven of the seventeen cases in which the lesion involved the esophagus alone, the patients were entirely asymptomatic. In contrast, in all cases in which the leiomyoma involved both the esophagus and the stomach, the patients had symptoms. The same was true of the patients with leiomyosarcoma.

Although, as Dr. Soutter has pointed out, the diagnosis of leiomyoma of the esophagus can usually be made with relative ease by means of roentgenographic examination and esophagoscopy, occasionally great difficulties are encountered. I was especially interested in the remarks of Dr. Soutter and Dr. Watson concerning the removal of tissue from a leiomyoma through an esophagoscope for microscopic examination. I may be wrong, but it is my opinion that it is not advisable to remove a specimen for biopsy from such tumors. In order to obtain tissue from the leiomyoma it is necessary to bite through normal esophageal mucosa which covers the tumor. Should the patient be operated on soon after such a specimen has been removed, and the tumor shelled out, the small hole in the esophageal mucosa made by removal of the specimen might escape detection and act as a possible source of mediastinal infection.

As stated previously, the diagnosis of leiomyoma is not always an easy matter and at times these tumors cannot be shelled out but must be removed by means of resection. A case in point at the Mayo Clinic was that of a young woman who suffered from dysphagia. The roentgenogram of the thorax showed the entire lower portion of the right side of the thorax to be infiltrated. Roentgenograms of the esophagus showed it was displaced to the right wall of the thorax. The correct diagnosis was not established until operation when it was found that the patient had a huge leiomyoma that involved the lower end of the esophagus and the cardiac end of the stomach, completely encircling both organs and displacing the esophagus to the right wall of the thoracic cavity. It was impossible to shell out the tumor, but resection was performed by Dr. Harrington with most satisfactory results.

DR. LEO J. KENNEY, Detroit.—I have been tremendously interested in the paper of Dr. Sweet and Dr. Soutter and also in the remarks of the other discussants. Within the past year I encountered a benign tumor of the esophagus which is probably the "Paul Bunyan" of all esophageal tumors. I would like to present this case.

(Slide.) This is a 17-year-old boy who had dysphagia for twelve years. He had been treated at several medical centers as a case of congenital shortening of the esophagus with cardiospasm. The slide illustrates the preoperative x-ray study. Shortly after these films were taken he developed complete obstruction of the esophagus.

(Slide.) This is an artist's reconstruction of the situation. The tumor completely encircled the esophagus. In order to remove it we had to open both the right and left chest. The tumor was adherent to the right lateral chest wall and to the right diaphragm.

(Slide.) This illustrates the extent of resection. The lower two-thirds of the esophagus, the upper third of the stomach, and the spleen were removed. An anastomosis was made above the aortic arch.

(Slide.) This shows the tumor itself. It measured 19 cm. in length, 15 cm. in width in the opened condition, and 7 cm. in thickness. It weighed 1,420 Gm.

(Slide.) The final slide shows the postoperative x-ray study, four months after operation. The upper segment remains dilated but there was no delay in the passage of barium and the boy is completely free of any swallowing difficulties.

DR. ROBERT M. JANES, Toronto.—In asking Dr. Sweet to close, I wonder if I might ask him a question. One very large tumor that was presented in Dr. Soutter's paper interested me, because I suspect that one of the patients in his table, on which there was an unsuccessful attempt at enucleation, was one that I helped Dr. Shenstone with at least fifteen years ago. The unsuccessful attempt, however, relieved the patient's difficulty in swallowing. The tumor extended to the diaphragm and the aortic arch and was at least 3 inches in diameter in a young girl 21 years of age. The symptoms dated back to childhood. She has since married and is well to date with very little change so far as we can determine by x-ray examination. I wonder if Dr. Sweet has any idea of the incidence of malignant changes in these tumors and whether it is ever wise to exercise discretion rather than valor.

DR. SWEET (Closing).—We were very hopeful that this paper would stimulate discussion and presentation of cases, and I can assure you that our expectations have been

amply justified. There is one preliminary point I would like to make before commenting briefly about the questions brought up, that is, that in going over the literature, and this applies to many of the cases mentioned here today, especially that of Dr. Janes, Dr. Soutter found that the literature was in an almost chaotic state. He has made a very earnest effort to find every possible report and case and has read, with one or two exceptions of inaccessible journals, every article that has been presented that he could find. It was interesting, for example, to find that one of our own cases, which had appeared in a report previously, appears in the literature as two cases, reported once by the pathologist and once by the surgeon. Things of this sort have occurred in many other instances. So we have attempted in this paper to bring a little order out of the chaos.

To turn to Dr. Meade's question, first of all I believe that the cases of Dr. Meade, Dr. Kay, and Dr. Daniels were reported in a summary by Drs. Myers and Bradshaw in THE JOURNAL OF THORACIC SURGERY in 1951; we must have missed it. I cannot answer Dr. Meade's question. I have no personal knowledge, and I do not believe Dr. Soutter has either, of why one should encounter necrosis in benign tumors of the esophagus enucleated from any particular segment. Of course we are all aware of the segmental nature of the blood supply. The only comment I can make about this is that I was consulted once about a patient who had had such an operation done on the upper portion of the esophagus where a fistula had resulted. Perhaps that was another instance of what Dr. Meade speaks of.

With regard to Dr. Higginson's interesting case, of which I was very pleased to hear, I suspect it was much like the one Dr. Soutter showed last in our series, a patient upon whom we have not yet operated. I must commend him for his exceedingly successful accomplishment. We have hesitated to operate upon our patient because of the enormous amount of esophagus involved and, as a matter of fact, he is getting along quite well as he is. There is more than one way of handling such problems.

Dr. Garlock, I am pleased to see, reported his series, a large one as these cases go. I do not agree with Dr. Garlock, however, on using esophagoscopy and esophagoscopic biopsy in these cases. In fact, I never use it in any case unless I feel that I cannot establish a diagnosis in any other way. His mention of the pedunculated nature of the malignant tumor is very important and emphasizes the importance of suspecting malignancy in some of these pedunculated tumors. I had a similar case which was reported as an adenoacanthoma with elements of epithelial malignancy as well as smooth muscle malignancy.

We are grateful to hear about Dr. Watson's interesting group. I am sure, however, that we would not have included his first case in our report because it was a fibrosarcoma and not a leiomyosarcoma, although it might be difficult to distinguish the two.

Dr. Moersch's experience is exceedingly interesting and valuable. We are pleased to have it presented in the discussion. It would seem to me, even with his large experience added to it, that we still do not have quite enough cases available to decide what the sex incidence is and why these tumors happen to be more common in one location than another. But I certainly heartily agree with Dr. Moersch about the inadvisability of obtaining biopsies in these cases, for the reasons he mentions and the technical difficulties and perhaps hazards which might result from previous injury to the mucosa at the time when the operation is to be done.

Dr. Kenney's case was of interest because one of our large tumors such as his was also treated for a long time with a diagnosis of cardiospasm. But he obviously has brought forth the leviathan of leiomyomas.

With regard to Dr. Janes's suggestion that the unsuccessful attempt at removal might be the one with which he had experience, I must say to our embarrassment that we did not know about his case. The one that was mentioned by Dr. Soutter was reported by Mr. Barrett of London. The patient died. With regard to the possibility of malignant degeneration in leiomyomas, we have no knowledge of that at all. I have always thought of these tumors in the same terms as we think of uterine leiomyomas, and of course we are all familiar with the fact that a few of them become malignant, but just how to pick the potentially malignant ones I am sure I do not know.

Dr. Soutter and I would like to thank all the discussers.

# REINFORCEMENT OF AORTIC ANEURYSMS BY WRAPPING

J. K. Poppe, M.D.
Portland, Ore.

CONSIDERABLE confusion seems still to exist regarding reinforcement of aortic aneurysms by external wrapping or patching. This confusion includes not only the modus operandi of the wrapping but also the nature of the material required and the sterilization of this material to prevent it from losing its irritating properties.

It is necessary to understand that the film employed represents merely a vehicle or structural framework for an irritating chemical which produces the fibrosis. Reinforcement of the aneurysm does not depend upon the tensile strength of the enveloping sheath nor upon the tightness of its application, nor necessarily upon the complete encirclement of the aneurysm. However, the greater the percentage of aneurysm surface covered the more effective the reaction. In clinical practice it is rarely possible to encircle completely large aneurysms which already are eroding into the spine, sternum, or other adjacent structures.

Pierce[1] has reported evidence of Cellophane bands cutting through the aorta of a dog when applied too tightly. An earlier report[2] of experimental work in 1946 indicated that polyethylene film produced a greater fibrous tissue reaction around dogs' aortas than the various types of Cellophane tested. These tests were conducted to determine which type of material produced the greatest fibrosis and constriction, since the literature contained a number of conflicting experimental and clinical reports on the subject. A supposedly inert plastic film called polyethylene was included among the types of Cellophane or cellulose hydrate and acetate. Much to our surprise the most extensive fibrosis was produced by the polyethylene which was said to be 99 per cent pure. Due to trade secrets it was impossible to identify the nature of the contaminant at that time, but Yaeger and Cowley[3] finally discovered it to be dicetyl phosphate and demonstrated its irritating reaction. Considerable confusion arose from two sources. First, the failure to distinguish the plastic film polyethylene from cellulose film known as Cellophane, and second, the different experimental and clinical reactions produced by two different types of polyethylene manufactured by different processes. The melt cast method, which is now used almost exclusively, produces a completely pure polyethylene which can be left inside the body without causing any reaction.[4] The solvent cast method, which was used only experimentally by DuPont during the early stages of development of polyethylene in 1945, introduced dicetyl phosphate as a contaminant on the surface of the film in less than 1 per cent concentration. This type is known as N.V. 7-14 and represents the one which caused the fibrosis around the dogs' aortas.

Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

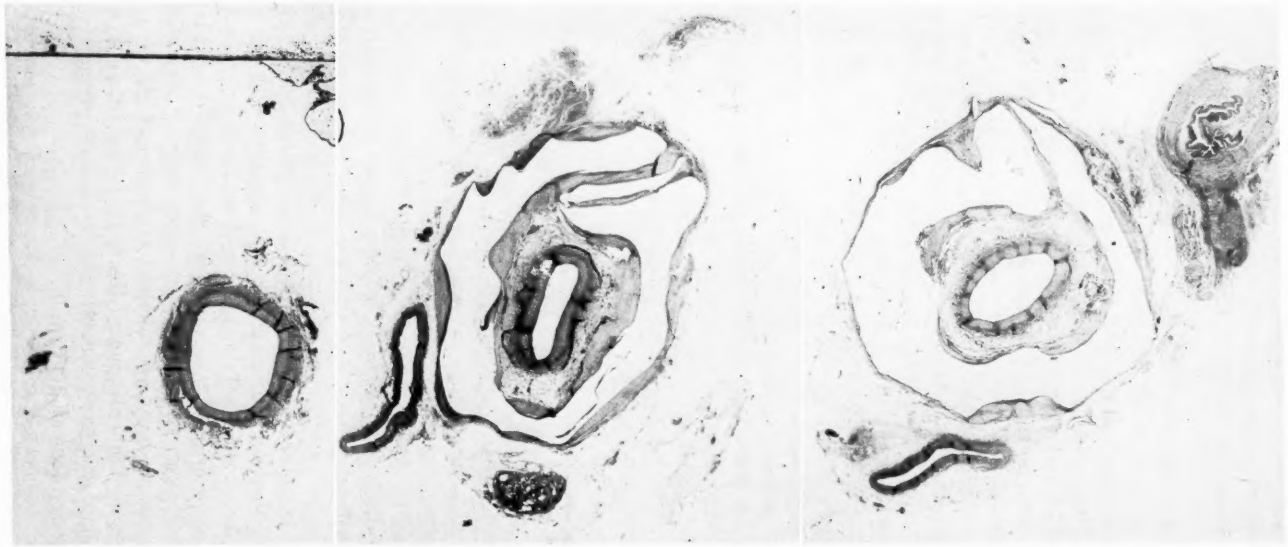
The inconsistent results obtained with Cellophane would appear to be due to the fact that it is manufactured for the packaging trade rather than the medical profession and is covered with a number of different sizings to meet the demands of self-sealing and vending machines. These sizings seem to greatly influence the tissue reaction but may be lost in the process of sterilization, depending upon the firmness of anchorage.

This same problem, of losing the active ingredient or dicetyl phosphate from the polyethylene, has arisen in the process of its sterilization and has undoubtedly reduced its effectiveness when improperly sterilized. Neither dry heat sterilization nor boiling is desirable since polyethylene has a melting point of 120° C. and dicetyl phosphate a melting point of 72° to 73° C. Thus, even though the original shape of the film may be partially retained after boiling a large percentage of the dicetyl phosphate has been lost in the water. Cold chemical sterilization remains as the most practical method and even this may cause loss of phosphate if the wrong solution or if too long a period of immersion is used. Dicetyl phosphate[5] is known to be slightly soluble in cold water and more soluble in alcohol, the rate of solubility increasing with the temperature and concentration of the alcohol. It is also soluble in benzene, toluene, butyl ether, and olive oil.

Analyses of the phosphate remaining on the polyethylene film and the amount lost in the sterilizing medium were made by Todd of the Biochemistry Department of the University of Oregon Medical School after immersing the film in different sterilizing agents for varying periods of time. Polyethylene film soaked for one week in 70 per cent alcohol lost 97 per cent of its dicetyl phosphate. Film soaked for one week in 1:1000 aqueous Zephiran solution lost 92 per cent of its dicetyl phosphate. Film boiled for ten minutes in water lost 40 per cent of its phosphate. Film soaked twenty minutes in 1:1000 Zephiran lost 16 per cent of its phosphate. Soaking the film in a cold aqueous solution of strong bacteriocidal agent for as short a time as is consistent with good aseptic technique appears to represent the best method of sterilizing the material without losing its active principle.

The solubility of dicetyl phosphate in sterilizing solutions and the insolubility of polyethylene in the body led to a search for another combination with opposite physical properties. Gelfoam film was substituted for polyethylene as a vehicle for irritating substances, but the Gelfoam disintegrated so rapidly when brought in contact with tissue juices that it proved to be technically impractical to handle, either as impregnated sheets or as a thin bag containing the powder. Talc, such as was formerly used for surgical glove powder, and powdered asbestos were impregnated on the surface of polyethylene film and a moderately satisfactory reaction was obtained. The perivascular fibrosis produced by talc and asbestos was not as dense as that produced by dicetyl phosphate during the short period of observation of two to four months employed experimentally in these dogs. Asbestos produced a more profuse reaction than did talc.

Injections of dicetyl phosphate in a .9 per cent solution in olive oil, as recommended by Berman and his associates,[6] has been used in inaccessible areas



*A.* *B.* *C.*

**Fig. 1.**—Three sections of abdominal aorta of dog sacrificed three months postoperatively. *A*, Control; *B*, wrapped with polyethylene impregnated with powdered asbestos; *C*, wrapped with polyethylene impregnated with powdered talc such as was formerly used in surgical gloves.

behind thoracic aneurysms. This method appears to be useful in conjunction with wrapping but has definite limitations when used alone. The presenting portion of the aneurysm, which has the thinnest wall and bulges out into the body cavity with little if any covering, offers no safe place for the insertion of a

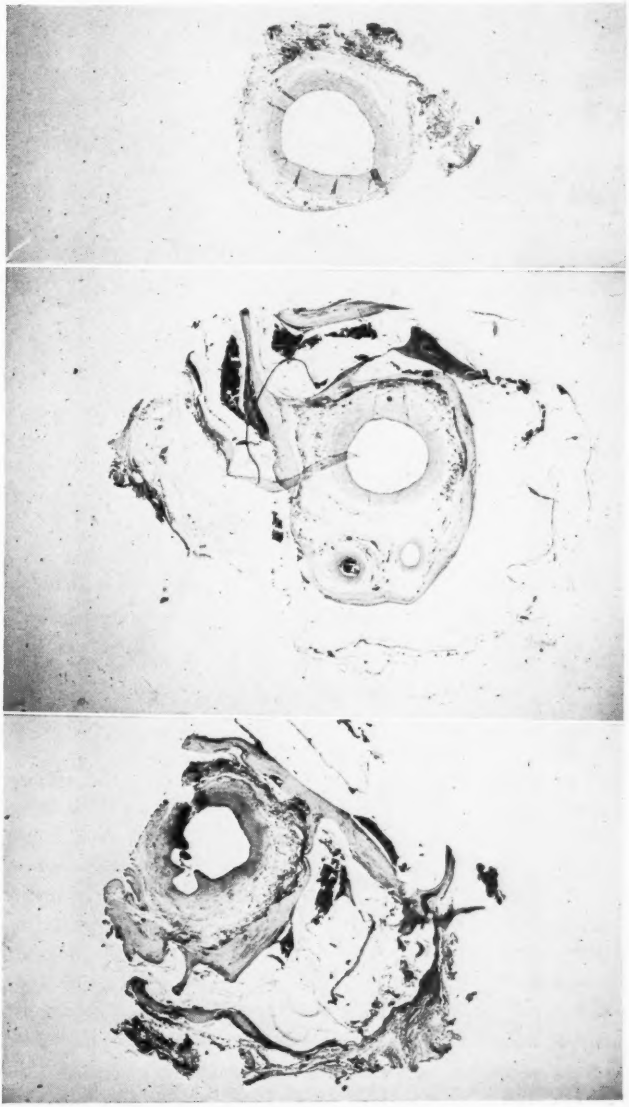
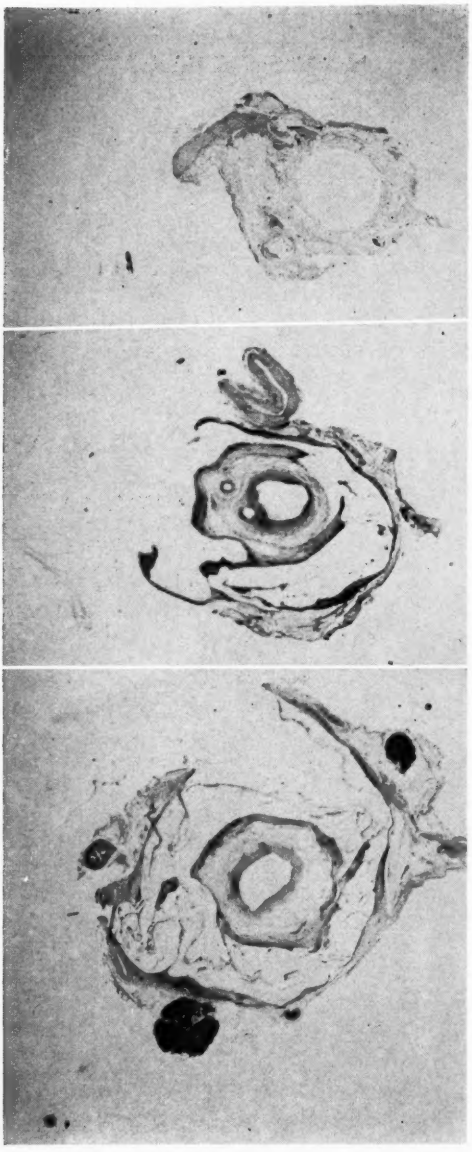



Fig. 2.—Three sections of abdominal aorta of dog sacrificed three months postoperatively. *A*, Control; *B*, wrapped with polyethylene covered on inside only with dicetyl phosphate. *C*, Wrapped with polyethylene covered on both sides with dicetyl phosphate.



*A.*

*B.*

*C.*

Fig. 3.—Three sections of abdominal aorta of dog sacrificed three months postoperatively. *A*, Control; *B*, wrapped with polyethylene covered on both sides with dicetyl prosphate, sterilized by boiling ten minutes. *C*, Wrapped with polyethylene covered on both sides with dicetyl phosphate, soaked for thirty minutes in 1:1000 aqueous Zephiran.

needle. This method does not include freeing of the pleura or peritoneum along the sides of the vessel which represents the first step in preparation for wrapping and relieves a great deal of the preoperative pain. The tendency for the oil to leak out into the pleural cavity has made me hesitate to use it around abdominal aneurysms where diffuse peritoneal adhesions would be quite undesirable.

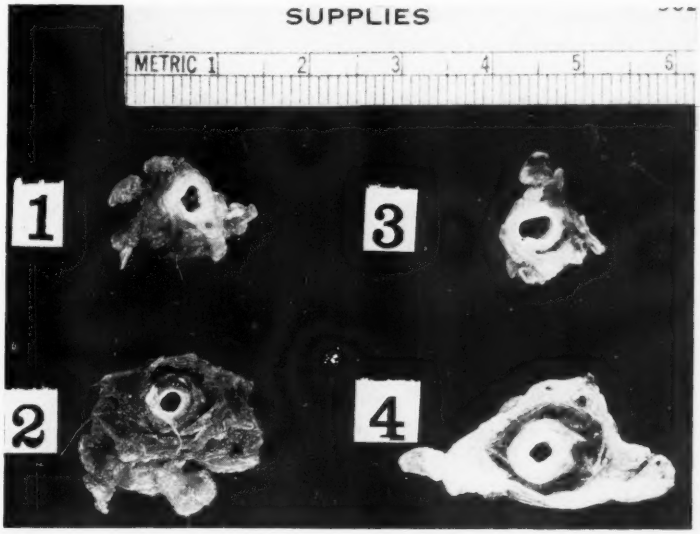



Fig. 4.—Photographs of gross specimens of aorta of two dogs sacrificed three months postoperatively. *1* and *3*, Controls; *2*, wrapped with polyethylene covered on both sides with dicetyl phosphate, sterilized by boiling ten minutes. *4*, Wrapped with polyethylene covered on both sides with dicetyl phosphate, sterilized by soaking thirty minutes in 1:1000 aqueous Zephiran.

Repeated animal experiments during the past five years have indicated that the greatest perivascular fibrosis is obtained by using polyethylene film which is heavily impregnated with dicetyl phosphate on both sides, as contrasted with the DuPont film which has only a small amount of phosphate on one side. The application of nonreactive Cellophane around the outside of the polyethylene, as once suggested, tends to limit the fibrosis sufficiently to interfere with the purpose of the wrapping.

The most effective preparation has been melting the dicetyl phosphate on the surface of the film. This can be done by either one of two methods. One method consists of spreading a thin layer of dry dicetyl phosphate powder evenly over the surface of a sheet of film and drawing this slowly over an electric plate until the powder has settled into the softened film. The other method requires passing the film through molten dicetyl phosphate. This latter method lends itself better to mass production techniques and permits a higher concentration of dicetyl phosphate but does not provide as firm an anchorage of the coating. It must be remembered that 120° C. is the melting point of polyethylene and

72° to 73° C. is the melting point of dicetyl phosphate. The electric plate should be just warm enough to melt the powder and soften the film without melting holes in the film.

Other methods of coating the film have been recommended, such as immersing the film in benzene containing dicetyl phosphate. Cold hydrocarbons cause polyethylene to swell and the dicetyl phosphate theoretically should become impregnated into the surface. Experiments to date have not indicated a very satisfactory fixation of the phosphate to the film surface by this method. The dicetyl phosphate has a tendency to rub off on handling the dry film.

Laboratory and clinical experience with wrapping, patching, and wiring aneurysms has indicated that the application of polyethylene film containing dicetyl phosphate represents the most satisfactory method of treating aortic aneurysms.[7] Admittedly, the film can rarely be placed completely around the aneurysm; it does not reduce the size of the aneurysm, it does not prevent the extension of the aneurysm with rupture in another area, and does not prevent rupture under the patch for a period of from four to six weeks postoperatively. Wrapping is best suited to fusiform aneurysms of the descending aorta below the arch where large branches are less numerous. Even with these limitations, wrapping affords a greater chance for relief of symptoms, prevention of rupture, and avoidance of fatal operative complications to a greater number of patients than any other method except resection.

## CONCLUSIONS

1. Polyethylene film wrapped around an aneurysm merely acts as a support for a chemical irritant which causes fibrosis and thickening.

2. Dicetyl phosphate heavily applied to both surfaces of polyethylene film represents the most satisfactory irritant.

3. Melting the dicetyl phosphate into the surface of the polyethylene provides the most permanent anchorage.

4. Chemical sterilization of the film for twenty minutes in 1:1000 aqueous Zephiran solution has proved satisfactory without excessive loss of dicetyl phosphate.

5. Heat sterilization disturbs both the polyethylene and the dicetyl phosphate.

6. Prolonged soaking in any solution reduces the dicetyl phosphate concentration on the film.

7. External reinforcement of aneurysms by wrapping represents the most effective method of treatment to aneurysms unsuitable for resection.

Acknowledgment is hereby given for the valuable assistance provided by the University of Oregon Medical School, Washington University Medical School, The Oregon Heart Association, and the following physicians: H. Renault, W. Ochs, J. Hessel, T. Gianelli, and J. Kane. W. R. Todd generously contributed his services in chemical analysis.

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## DISCUSSION

DR. WILLIAM A. HOPKINS, Atlanta.—We, too, have been much interested in the use of Cellophane in thoracic and abdominal aneurysms. At first, at the suggestion of Dr. Poppe, we used Cellophane as prepared by the DuPont Company with such variable results that we were not entirely satisfied with this method. However, I wish to report three later cases in which we used Cellophane. We impregnated with a suspension of dicetyl phosphate that was painted on the Cellophane at the time of surgery. This method was described by Dr. Hufnagel. This had some disadvantage because it cracks off very easily at the time of surgery and some of the dicetyl phosphate may therefore be deposited about the thoracic cavity. We feel it is too soon at the present time to make any definite conclusions as to results. There is one additional point I would like to bring up: we have also wrapped aneurysms of the ascending aorta. We feel that in our first cases there were considerable amounts of irritation within the pericardium, which produced arrhythmias that were very difficult to handle. If the outer surface of the Cellophane is wrapped with nonreactive Cellophane this complication can be alleviated.

DR. GEORGE H. HUMPHREYS, New York.—At the Presbyterian Hospital in New York Dr. Blakemore has been interested in treating aneurysms for a number of years, as I am sure you know. His method has consisted primarily of wiring and electrocoagulation, but since the first reports of the use of reactive Cellophane this method has also been used. We have been disturbed not only by the inconsistencies in reaction, on the subject of which Dr. Poppe has helped us a great deal with his presentation, but we have also been disturbed to learn from Dr. Oppenheimer, at the Cancer Institute, that fibrosarcomas can be produced in rats with this agent. This fact, although rats are not human beings, seems to us a reason for hesitation. There is a further theoretical consideration. Treatment of aneurysms by this method, as Dr. Poppe himself has mentioned, is very limited in certain respects. It has perhaps more analogy to the treatment of hernia by injection and sclerosing agents. A fibrotic reaction can resist an expanding tendency to a certain extent, but only to a limited extent. Recently, Dr. Deterling has tried another approach in the laboratory, using a nonreactive, nylon mesh, wrapping vessels, particularly grafted vessels, in order to prevent their late expansion into aneurysms. This has proved very effective, at least in the experimental animal, and we are beginning its use in human beings.

DR. DENTON COOLEY, Houston.—On the basis of our clinical experience with the polythene dicetyl phosphate film, which was obtained from the DuPont de Nemours and Company, we agree with Dr. Poppe that insufficient fibroplasia is produced by this untreated film to which additional irritant has not been added. Recently, Dr. DeBakey and I have reexplored two of our patients in whom an abdominal aortic aneurysm had previously been wrapped. In both instances symptoms persisted and pain increased, and the aneurysm had definitely enlarged. Although periods of thirteen and eight months, respectively, had elapsed, in neither patient was there evident exuberant fibrosis. The polythene film had been prepared by soaking in 1:1000 aqueous zephiran solution for twenty to thirty minutes.

(Slide.) This is a color photograph showing the application of the film in December, 1951, to an abdominal aneurysm. In July, 1951, a large sacciform aneurysm of the

innominate artery was excised in this same patient and there has been no recurrence of this lesion.

(Slide.) In this photograph the condition of the abdominal aneurysm at the second laparotomy in January, 1953, can be seen. The polythene film is encased in a paper-thin membrane of fibrous tissue. Indeed, the wall of the aneurysm itself appeared necrotic, as if the film of polythene had served to deprive the adventitial layers of vascular supply.

(Slide.) In this photomicrograph made from tissue forming the wall of the aneurysm and polythene film, one is impressed by the relatively slight amount of fibrosis produced. Similar findings were present in the patient re-explored eight months after the wrapping procedure.

We are becoming increasingly skeptical of the efficacy of so-called fibroplastic agents in the treatment of aneurysm. Excision of the aneurysm with restoration of vascular continuity appears to be the procedure of choice, and we feel that it can be done in the majority of cases. I disagree with Dr. Poppe when he refers to wrapping and wiring of aneurysms as ideal treatment. I consider such methods as compromises with ideal therapy, which should be surgical excision.

DR. POPPE (Closing): Dr. Hopkins' comment about protecting adjacent vital structures around an aneurysm is well taken, but I prefer to use a layer of tissue, such as pleura, fat, or omentum, over the polyethylene film rather than adding a layer of non-reacting Cellophane. It is also necessary to distinguish polyethylene, which is a polymer of ethylene, from Cellophane which is a cellulose product. A one-sided reaction can be obtained with polyethylene by coating only one side of the film with dicetyl phosphate as was done with the DuPont film N.V. 7-14. Experimental work indicates the desirability of obtaining as much reaction as possible and this reaction is greatly reduced by eliminating or covering up the irritant on one side of the film.

Dr. Humphrey's suggestion about reinforcing aneurysms with nylon mesh around the outside is very interesting and should give a great deal of support if it can be used to completely encircle the aneurysm. My experience would indicate that the majority of large aortic aneurysms are already eroding into some adjacent structure, such as the spine or sternum and cannot be completely encircled, thereby limiting the usefulness of this method.

Dr. Humphrey's report about dicetyl phosphate causing fibrosarcoma in mice is somewhat disturbing, but I doubt if any of these patients with aortic aneurysms will survive the fifteen to twenty years which would probably be required for the development of malignancy. Some other irritant, such as asbestos or talc, could be substituted for the dicetyl phosphate.

Dr. Cooley's remarks about resection being the ideal treatment may apply to a limited number of aneurysms, but I still believe that wrapping is the treatment which is applicable to the greatest number of patients with the disease. I am sure that at least 90 per cent of the aneurysms I see could never be resected. Three of these aneurysms have ruptured spontaneously during the past three months within twenty-four hours after being seen. Better preparation of his polyethylene should improve his results with wrapping.

I wish to thank the discussants for their very interesting and informative comments on this difficult problem of treating aneurysms of the aorta.

# ENZYMATIC DÉBRIDEMENT

## Particular Reference to Tryspin and Desoxyribonuclease in the Control of Cough and Sputum Associated With Tuberculosis*

Seymour M. Farber, M.D. (by invitation), R. Daniel Gorman, M.D. (by invitation), David A. Wood, M.D. (by invitation), Orville F. Grimes, M.D. (by invitation), and Samuel L. Pharr, B.S. (by invitation)
San Francisco, Calif.

IN ANY chronic infection, the collection of fibrin, degenerating cells, and the purulent exudate that soon appears considerably inhibits therapeutic measures. In the past, it has generally been necessary to clean such areas, when possible, by repeated surgical débridement. Except in superficial infections, débridement was frequently unsatisfactory and sometimes impossible. In many cases permanent disability, and even death, have been directly attributable to this technical problem.

Recently the streptococcal enzymes, streptokinase and streptodornase, and the pancreatic enzyme, trypsin, have been utilized for débridement. All these agents act to the same end, the digestion of fibrin and necrotic products, and none of them, in therapeutic doses, inhibits the growth of new granulation tissue. Thus, the risk that superficial trauma will delay healing is avoided.

Until recently, interest in the use of these enzymes in the management of chest diseases had been limited to their usefulness in the treatment of pleural conditions (empyema and hemothorax) and infections of the chest wall sinuses. There is reason to hope, however, that one of these agents, or some related compound, will eventually be useful in the management of a number of chronic chest diseases. One of them, tryspin, has already been applied to the débridement of the bronchial tree. Because few reports on this type of application have appeared, our own experience with bronchial débridement will be discussed in some detail later.

### STREPTOCOCCIC ENZYMATIC DÉBRIDEMENT

In 1933, Tillett and his associates[1, 2] discovered that hemolytic streptococci, when cultured, excreted an enzyme, streptokinase, into the culture medium, which acted upon fibrin and markedly promoted the dissolution of human blood clots. In 1948, a second enzyme was demonstrated to be the product of the same bacteria.[3] This enzyme acted upon desoxyribonucleoprotein, which is largely responsible for the characteristic viscosity of purulent exudates. The first enzyme, streptokinase, was found to act indirectly; it converted plasminogen in human blood into plasmin, which in turn dissolved insoluble fibrin into

From the Cancer Research Institute and the Departments of Medicine and Surgery, University of California School of Medicine; and the San Francisco Department of Public Health (San Francisco Hospital).

Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

*The trypsin (Tryptar) and desoxyribonuclease used in this study were kindly furnished by the Armour Laboratories, Chicago, Ill.

soluble proteins. The second enzyme, streptodornase, was found to be composed of a series of closely related enzymes which acted directly upon desoxyribonucleoprotein. At the present time, these two enzymes are used in combination, four units of streptokinase to one of streptodornase.

A number of studies on the application of this enzyme combination in various thoracic conditions have been published. DeBakey[4] reported the combination particularly effective in the treatment of infected hemothorax. He found that it produced marked thinning of the exudate and dissolution of loculations; and, in many instances, it obviated the need for thoracotomy. Tillett, Sherry, and Read[5] emphasized the value of streptokinase and streptodornase in the treatment of tuberculous empyema. They observed that the enzymes not only reduced the viscosity of the pleural fluid, but contributed directly to sterilization of the pleural space. In general, streptokinase and streptodornase appear to be of proved service in the treatment of any condition in which an accumulation of viscous pleural fluid interferes with other types of therapy. At the same time, it should be recognized that additional clinical work is required to establish the conditions under which optimum results can be anticipated.

### TRYPSIN DÉBRIDEMENT

Trypsin is a pancreatic enzyme whose lytic action on mucus and fibrin has long been recognized. It has only recently, however, become available in a sufficiently purified form to be used clinically. Like the streptococcic enzymes, its obvious application in thoracic medicine lies in the treatment of pleural complications, and the range of its reported usefulness closely parallels that of streptokinase and streptodornase. Roettig and his associates[6] emphasized in particular the effective sterilization of the pleural space obtained with trypsin; they concluded that the sterilization that followed treatment in fifteen of sixteen cases of empyema, including tuberculous empyema, was due in great part to the action of the enzyme. These investigators attributed this antibacterial effect to the digestion of the pus and debris which apparently are necessary for growth of bacteria in pleural fluid. Also, of course, the decrease in viscosity of such fluid effected by the enzyme permits more efficient antibacterial action by humoral defense mechanisms.

### BRONCHIAL DÉBRIDEMENT

The necessity for new measures for the management of pulmonary tuberculosis has become obvious. Despite recent progress in surgical and antibiotic therapy of this disease, the control of symptoms, particularly the large quantities of sputum and excessive cough, remains a problem. Since use of cough suppressants often leaves much to be desired, considerable effort has been expended in the past ten years to find a more satisfactory means of treatment. These considerations are emphasized, we believe, by results of our own attempts to utilize trypsin to control the cough and heavy production of sputum associated with pulmonary tuberculosis.

Logically, administration of trypsin by aerosol inhalation should aid in the control of these symptoms. Limber and his co-workers,[7] in the first pub-

lished study of the effect of this enzyme on abnormal bronchial secretions, concluded that trypsin was of value in the treatment of a number of pulmonary conditions. Our early trials with trypsin alone, however, demonstrated that the action of trypsin seems to be confined to mucus, fibrin, and noncellular material. Since the viscosity of purulent sputum is largely due to its high content of desoxyribonucleic acid, it was felt that trypsin might profitably be supplemented with desoxyribonuclease, a pancreatic enzyme which had been demonstrated specifically to depolymerize desoxyribonucleic acid in in vitro studies.[8]

*Selection of Patients.*—The twenty-four patients included in this study had excessive cough and consistently raised large quantities of sputum. The majority had far-advanced pulmonary tuberculosis, and had undergone collapse procedures, as well as treatment with antibiotic and chemotherapeutic agents. A few patients, however, were given trypsin shortly after hospitalization and before any specific therapy was instituted. Four of the twenty-four patients had associated bronchiectasis, suspected or proved; four had tracheobronchial tuberculosis; and four had marked emphysema and bronchial asthma. One patient had a coexistent pulmonary neoplasm proved by cytologic studies of the sputum.

*Technique.*—Trypsin was administered by aerosol inhalation. The most satisfactory method was by means of a Vaponefrin nebulizer, which consisted of the nebulizer itself, a rubber bag containing hot water to humidify the aerosol mixture, and a nosepiece. By this approach, the nose acts as a baffle, removing the larger drops of moisture which are usually the chief source of bronchial irritation. No irritation of the larynx or throat was noted with this method of administration, although such irritation had been a serious problem at the beginning of the study when an ordinary mouth nebulizer was used. Nasal irritation was minimized by the application of petroleum jelly prior to inhalation and a thorough rinsing of the nose and throat immediately afterward.

*Materials.*—Dosage and length of administration varied. At the beginning of the study each patient received 1,000 Armour units of trypsin daily, but it was rapidly demonstrated that doses of 100,000 units could be tolerated; later, the dose was increased to as much as 100,000 to 150,000 units daily. The course of treatment ranged from three to thirty-two days, with an average of ten days; several patients received more than one course of therapy.

The first eleven patients in the series were given one course of trypsin alone. Sixteen patients were given desoxyribonuclease in addition to trypsin in doses ranging from 2 mg. daily for four days to 5 mg. daily for eleven days. One patient received 5 mg. of desoxyribonuclease alone each day for four days without apparent benefit.

Sorensen's buffered phosphate solution, in volumes not exceeding 2.5 c.c. per inhalation, was the diluent in most instances. On several occasions physiologic saline solution was substituted for the phosphate buffer solution, but it did not reduce the incidence of local reactions.

*Method of Evaluation.*—The primary interest was in the effect of these enzymes on cough and sputum production. Patients were carefully observed

during and after each course of inhalation, and each day sputum was collected, measured, and a record kept of volume and gross appearance. The usual standard clinical tests were performed on all patients.

In addition, the possible effect of trypsin and desoxyribonuclease on pulmonary function was carefully evaluated in six patients. The Warring method[9] was used, since our previous experience with 450 patients had convinced us that it provides a helpful index of variations of pulmonary function. None of the six patients showed a significant change in WV/M.B.C. ratio after administration of these enzymes. Cytologic examination of the sputum was performed in sixteen patients. Control sputum specimens were obtained before treatment to establish a typical "cellular picture" for each patient, and specimens were collected at intervals after treatment was begun for comparison and evaluation.[10-14]

*Results.*—The most favorable effects on cough and production of sputum were obtained by a combination of trypsin and desoxyribonuclease. Only three of the eleven patients who received a course of trypsin alone were noted to have a decrease in cough, whereas in the remaining eight patients, cough appeared to increase in severity. On the other hand, nine of the sixteen patients who received combined therapy showed a significant reduction in cough, and in three of these the response was marked.

Sputum was decreased in quantity by trypsin alone in four cases and by trypsin and desoxyribonuclease in six others. In the majority of patients, however, the amount of sputum raised was increased by therapy. Eleven of the sixteen patients who received the enzymes in combination believed that the raising of the sputum was noticeably easier following treatment.

Use of the combined enzymes resulted in a grossly evident decrease in both the viscosity and the purulence of sputum in eight instances, and in a decrease in viscosity alone in an additional two. In no instance, however, did trypsin alone effect a striking change in the gross appearance of the sputum.

*Toxicity.*—The frequency of mild irritative reactions following the administration of these enzymes has been noted. We were more impressed, however, by the number of moderate to severe reactions of various kinds, which occurred following administration of both trypsin alone and of trypsin and desoxyribonuclease. In the majority of cases the reactions obviously resulted from the local irritating effect of trypsin, and perhaps also of desoxyribonuclease. They consisted of hoarseness and aphonia, severe cough, and hemoptysis which occurred in seventeen (71 per cent) of the patients. Administration of the enzymes by nasal inhalation reduced the severity of the reactions and the incidence of local irritation, but twelve of twenty patients so treated still demonstrated appreciable side effects. In nine instances these reactions were so severe that the patients refused further inhalations.

The occurrence of generalized toxic reactions was of greater significance. The most common reactions were severe dyspnea and wheezing, which usually immediately followed inhalation, chills and fever, which appeared some four hours later, and a generalized rash. The incidence of these reactions was not affected by the method of administration.

Three patients developed chills and fever following aerosol inhalations. One patient's temperature rose to 104° F. on five occasions, after which treatment was discontinued. Another patient developed a morbilliform rash after completion of a series of inhalations. This rash was most severe on the trunk and decreased toward the extremities. It disappeared gradually over a period of two weeks.

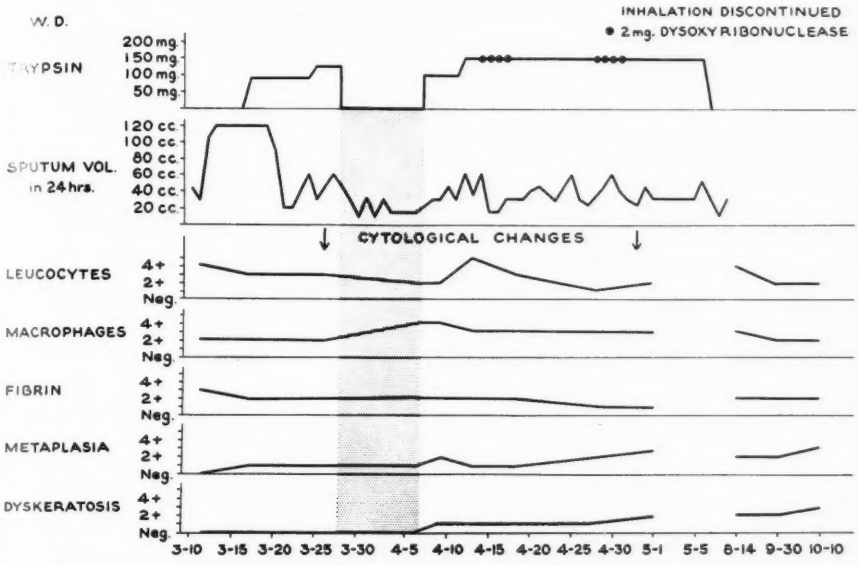


Fig. 1.—Cytologic changes in a patient (W. D.) receiving trypsin and desoxyribonuclease by inhalation.

*Cytologic Findings.*—Cytologic studies failed to show any evidence of destruction or lysis of formed elements in the sputum or any alteration in fibrinous elements. Enzyme therapy did, however, affect the quantity of macrophages and inflammatory cells in the sputum (Fig. 1). This response followed a definite pattern: the sputum showed a sharp increase in the number of macrophages and inflammatory cells during the first two hours after inhalation, followed by an abrupt decline toward preinhalation levels. The number of cells again increased gradually for a period of days, then dropped slowly back to preinhalation levels. We cannot account for this specific pattern, although the increase in inflammatory cells and macrophages would seem to be an irritative response.

In twelve of sixteen patients cytologic examination of the sputum showed changes in exfoliated epithelial cells which were consistent with bronchial metaplasia and dyskeratosis (Figs. 2 to 4). These alterations consisted of enlargement of nuclei with vacuolization and increased keratinization of the cytoplasm. The abnormal cells appeared soon after trypsin inhalation was begun and have

persisted to the present time, despite discontinuance of therapy. We are unable to evaluate fully the significance of these observations, but additional studies are indicated.

*Discussion.*—Although in a majority of the patients in this series, some decrease in severity of cough and in viscosity of sputum followed enzyme therapy, our own results were considerally less impressive than those obtained by Limber and his associates.[7] Further, it was our impression that desoxyribonuclease was an essential factor in the improvement noted. Our most consistent finding was decrease in sputum viscosity. In most instances, however,

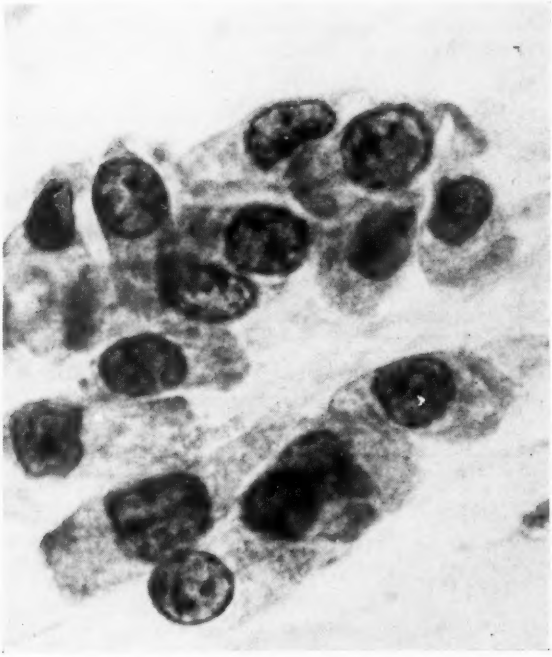

Fig. 2.—Typical bronchial epithelial cells (×776).

there was an actual increase in the production of sputum, whereas Limber found a decrease. It must be remembered, of course, that the Limber cases included a variety of pulmonary conditions; our patients had pulmonary tuberculosis as the primary disease process in every instance. In addition, antihistamines were used sparingly in our patients.

The most striking difference between our results and those previously reported was the frequency of moderate to severe reactions to enzyme administration in our patients. Although considerable local irritation was eliminated by the use of a Vaponefrin nebulizer, nevertheless twelve of the twenty-four patients given enzymes by nasal inhalation were found to have side effects of one kind or another.

Fig. 3.

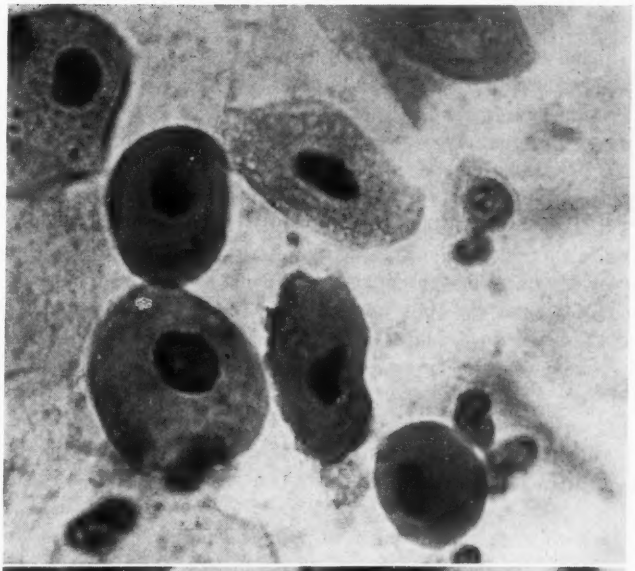

Fig. 4.

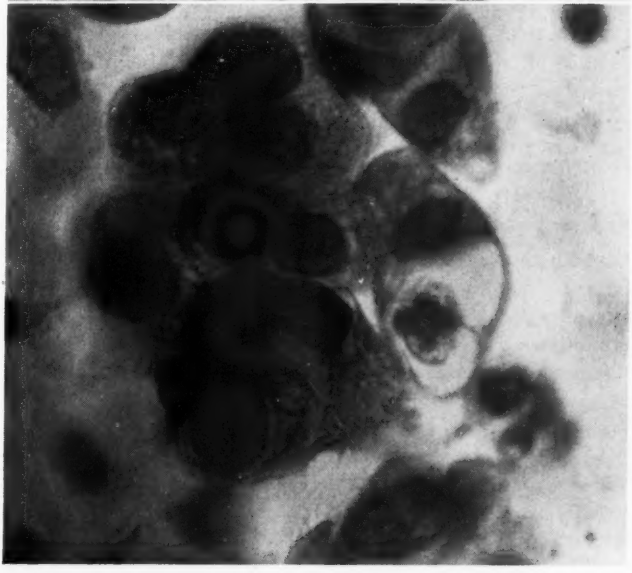

Fig. 3.—Typical metaplastic cells (×776).
Fig. 4.—Atypical cells observed in sputum of W. D. following inhalation of trypsin and desoxyribonuclease (×776).

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The most serious of these effects was the development of a typically asthmatic episode of wheezing and dyspnea. Once a patient experienced such an attack, additional therapy generally resulted in increasingly severe reactions. Continued treatment was possible in only one of eight patients in whom this reaction developed. Pyribenzamine had no effect upon this tendency in any of the three patients receiving it. The episodes of chills and fever that developed in three of twenty-four patients were equally serious. In two cases, these episodes were isolated instances; in the third patient, they were invariable.

The asthmatic attacks obviously represented a specific sensitivity. It is likely that the chills and fever were a different manifestation of the same phenomenon, although they may have resulted from absorption of products of enzymatic digestion. Such absorption would have much the same effect at the intravenous injection of partially digested protein products. It is perhaps worth noting that the repeated episodes of chills and fever occurred in one of the few patients in whom the therapy was markedly effective in reducing cough and thinning sputum.

Last, four patients who had no previous history of hemoptysis noted blood streaking of the sputum ten days or more after inhalation was begun. Although of little importance in itself, since the amount of blood raised was small, this symptom gave further evidence of the toxicity of these compounds. Reiser and his co-workers[16] noted a similar phenomenon in their treatment of empyema cavities with trypsin; hemorrhagic pleural fluid frequently appeared from four to seventeen days after instillation was begun.

On the basis of these studies, we have concluded that trypsin and desoxyribonuclease should not be recommended for routine use in the treatment of tuberculous patients with productive cough. A few of our patients seemed to show a distinct long-term improvement and the majority benefited temporarily, but it was felt that the toxicity of these compounds outweighed their beneficial effects.

These objections are obviously not insurmountable. Bowman[17] reported that iodinated trypsin does not have the marked hypotensive effect on dogs that trypsin has; other modifications would seem to be possible. Of great interest is the recent announcement of a preparation of trypsin of such low toxicity that it may be administered intravenously.[18] When such a product becomes generally available, it may well remove present objections to the use of the enzyme. It will also be necessary to evaluate the cytologic findings herein reported.

## SUMMARY AND CONCLUSION

Two enzyme products, trypsin and a combination of streptokinase and streptodornase, have recently been applied to the problem of débridement of various kinds of chronically infected areas. In the field of chest disease they have been chiefly of value for their possible contribution to the management of empyemas and postoperative or traumatic hemothorax.

It is emphasized that the addition of enzymes to this kind of therapy is still in the developmental stage and it should be approached with caution. This is confirmed by our own use of trypsin for bronchial débridement. Twenty-four

patients with pulmonary tuberculosis who had excessive cough and who were raising moderate to large amounts of sputum were given trypsin alone or in combination with desoxyribonuclease by aerosol inhalation. Trypsin alone was of little effect but, in combination with desoxyribonuclease, it reduced cough and viscosity of sputum in a majority of cases. Results were not marked, however, except in three patients who showed a substantial decrease in cough. Almost three-fourths of the patients in the series had significant reactions. Sensitivity reactions in the form of chills and fever or asthmatic attacks were encountered. Cytologic studies of the sputum of sixteen patients revealed increased metaplasia in the cellular components in twelve of them.

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## DISCUSSION

DR. C. THOMAS READ, Phoenix.—When I came to this meeting I said to someone that I was not going to mention anything about varidase or streptokinase or streptodornase. However, after hearing this rather exciting paper and the excellent work demonstrated by Dr. Farber, I arise mainly to ask him if a comparable control study was run at the same time with varidase. Trypsin was available to Dr. Sherry in the early part of our studies, and we too found quite a decided reaction when the agent was instilled into the bronchus mainly by aersol therapy.

Recently Winthrop-Stearns, Inc. has manufactured a product known as Alevaire, of which they sent me a quantity for clinical trial before it was released to the profession. It formed a good vehicle for varidase if a patient had indicated symptoms for such aerosol therapy. Antibiotic agents can be used with Alevaire and also varidase and aerosol therapy thereby given, which will reduce the purulent character of sputum. I mention the purulent character because it was shown that purulent exudates contain about 30 to 70 per cent of nucleoprotein and these are the elements which are affected by varidase. If the sputum or exudates are mucinous in character, varidase is not effective. That seems to be the advantage of trypsin or the pancreatic enzymes, lacking in varidase.

I would like to ask Dr. Farber also if the desoxyribonucleoprotein element, its amount and so on, was demonstrated in the exudates they were studying.

DR. DUANE CARR, Memphis.—Dr. Read has already mentioned a product with which we are now working, Alevaire, as an adjunct to the treatment for the reduction of sputum, particularly in the preparation of patients for surgery. This product is thoroughly applicable to the tuberculous patient as well as the one with suppuration or a very purulent bronchiectasis.

Its one possible theoretical disadvantage, which remains to be determined, is the fact that it acts as a wetting agent, reducing surface tension, which is advantageous in improving the ability of the patient to raise his sputum, but may prove a disadvantage because of the drying effect within the lung itself.

We all know that the contractility of the lung is in part due to surface tension of the moisture lining the alveolar air spaces. We also know that in the patient with emphysema one of his principal difficulties is the lack of contractility of his lung, so that Alevaire cannot yet be used with complete confidence in the emphysematous patient. Symptomatically, it is extremely effective and can be used as a vehicle for the appropriate antibiotics if the use of aerosol therapy is desired. Its effect is particularly striking in the bilateral purulent bronchiectatic patients who, in some instances, may be raising as much as one pint of sputum per day. When the patient is placed upon a routine of aerosol inhalations of appropriate antibiotics and Alevaire three or four times a day, combining it with the usual postural drainage routine, the regimen reduces sputum from one pint to as little as one ounce or one and one-half ounces, almost totally lacking in purulent elements.

We are very interested in the work of Dr. Read, Dr. Sherry, and Dr. Christensen in the use of streptokinase and streptodornase and have used it extensively for other purposes, particularly in the pleural cavity, but to date we are enjoying a very satisfactory result from the use of Alevaire with antibiotics and the postural drainage regimen.

DR. FARBER (Closing).—I very much appreciated the comments of Dr. Read. In the April, 1951, issue of the JOURNAL of this Association, there is an excellent paper, with Dr. Read as one of the co-authors, on the use of streptokinase and streptodornase in the treatment of empyema. The pioneer work in the entire field of enzyme therapy as applied to the thoracic cavity has originated in Dr. Tillett's group.

Dr. Read mentioned the use of Alevaire, and Dr. Carr has followed with very important suggestions as to the usefulness of this particular preparation. We also have received some, but our experience is most limited, and hence I was happy to hear these comments. As yet, Dr. Read, we have not carried out cytologic studies with streptokinase and streptodornase.

This work is in its early stages and should be repeated and carried forward in other cytologic laboratories.

# AN EXPERIMENTAL STUDY OF THE EFFECT OF PARASYMPATHETIC DENERVATION OF THE LUNG ON PULMONARY ARTERY PRESSURE

VICTOR H. KAUNITZ, M.D. (BY INVITATION), AND MURRAY N. ANDERSEN, M.D. (BY INVITATION)
BUFFALO, N. Y.

BECAUSE of the dearth of knowledge of the mechanisms regulating the lesser circulation, it was thought useful to study changes in the pulmonary vascular bed following complete parasympathetic denervation of the lung in the experimental animal. This study was facilitated by the availability of a measurement of complete parasympathetic denervation of a lung.

This test consisted of determining the presence or absence of the Hering-Breuer reflex unilaterally during bronchospirometry. Juvanelle,[1] working in our laboratory on bronchospirometry in dogs, found that after occluding the airflow from one lung at the end of expiration, the Hering-Breuer reflex was not activated. The animal continued to breathe normally without a period of apnea (Fig. 1). If the airflow was occluded at the end of inspiration, or if the lung was forcibly inflated, which was necessary occasionally when ventilatory volume was depressed by deep anesthesia, stretch receptors in the lung were continually activated. Inspiration was inhibited and apnea occurred (Fig. 1). The Hering-Breuer reflex, described originally in 1868 and measured in the isolated vagus fiber by Adrian[2] in 1933, was in operation. When enough carbon dioxide accumulated, or when the arterial oxygen level fell sufficiently, the respiratory center was stimulated, escaped from the inhibitory impulses, and respiration was resumed.

After vagus section in the neck, or division of all vagus branches to the lung, when that lung was inflated, there were no longer inspiratory-inhibiting impulses reaching the respiratory center. Normal respiratory rhythm continued without apnea (Fig. 1). The homolateral Hering-Breuer reflex had been abolished. This reflex was known to be transmitted via vagus afferent fibers from the lungs. It is assumed that vagus efferent impulses travel along the same pathways.[3, 4] Absence of the Hering-Breuer reflex would therefore indicate complete parasympathetic denervation of the lung.

## METHOD

Ten healthy mongrel dogs were studied by means of the described ventilatory test, and by cardiac catheterization preoperatively and after parasympathetic denervation of both lungs. Under intravenous Nembutal anesthesia, a specially constructed bronchospirometry tube was passed into the trachea with the animal in a supine position (Fig. 2). The tube was fastened in place and

From the Surgical Research Laboratory of the E. J. Meyer Memorial Hospital and the University of Buffalo Medical School.
Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

connected to a bronchospirometry apparatus which recorded a simultaneous tracing of the ventilation of both lungs. This apparatus was similar to that used in the human cardiopulmonary laboratory, except that the spirometer bells had a smaller volume. Presence of the Hering-Breuer reflex bilaterally was confirmed.

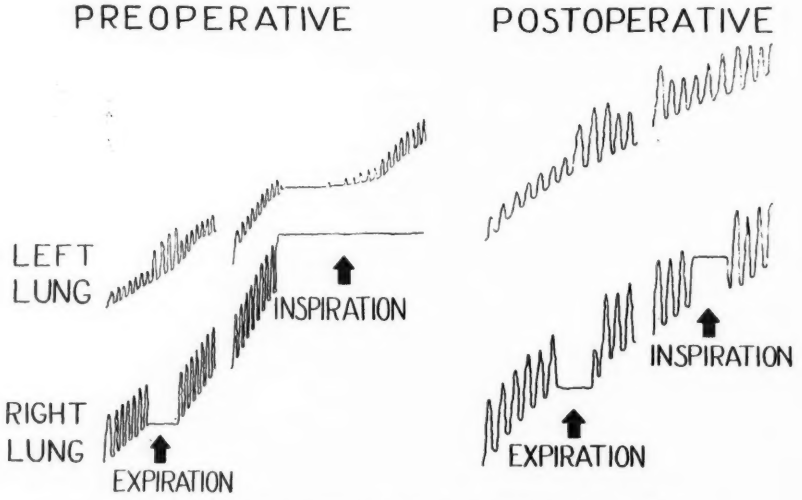



Fig. 1.—Effect of parasympathectomy on Hering-Breuer reflex.

Cardiac catheterization was then performed during the same anesthesia. The pulmonary artery was entered in all animals, and pressure recording was made during withdrawal of the catheter from a parenchymal branch of the pulmonary artery into the main artery and into the right ventricle. Pulmonary artery pressure was calculated in all cases from that part of the tracing just before the right ventricular pressure curve (Fig. 3).

Left thoracotomy was then done under intravenous Nembutal anesthesia. Alternating positive pressure controlled respirations were maintained by oxygen flowing through a Burns valve connected to an endotracheal tube. The vagus trunk was carefully isolated, and all branches to the lung were dissected free (Fig. 4, *B*). From ten to thirteen branches were found and divided. Thoracic cardiac nerves were preserved. The lung was then reinflated by manually squeezing a small rebreathing bag attached to the sidearm of the endotracheal tube. In this way all atelectatic areas of the lung were reaerated and complete re-expansion achieved.

After an interval of approximately four weeks, a right thoracotomy was done. Six to ten vagal branches to the lung were found on this side and divided (Fig. 4, *A*). In the last four dogs femoral arterial pressures were measured during the second operation to determine if this parasympathetic denervation

had any effect on cardiac output, as reflected in systemic pressure. After another four-week interval, each animal was again anesthetized, and the ventilation test and cardiac catheterization repeated.

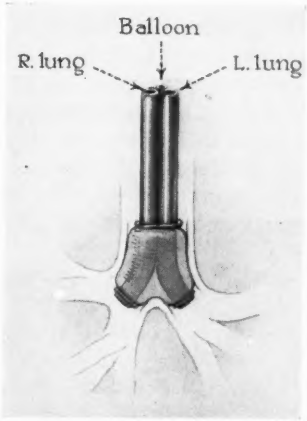



Fig. 2.—Positioning of the bronchospirometry tube in the trachea.

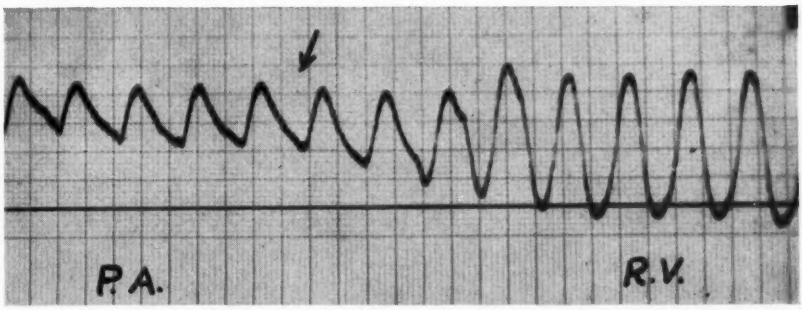


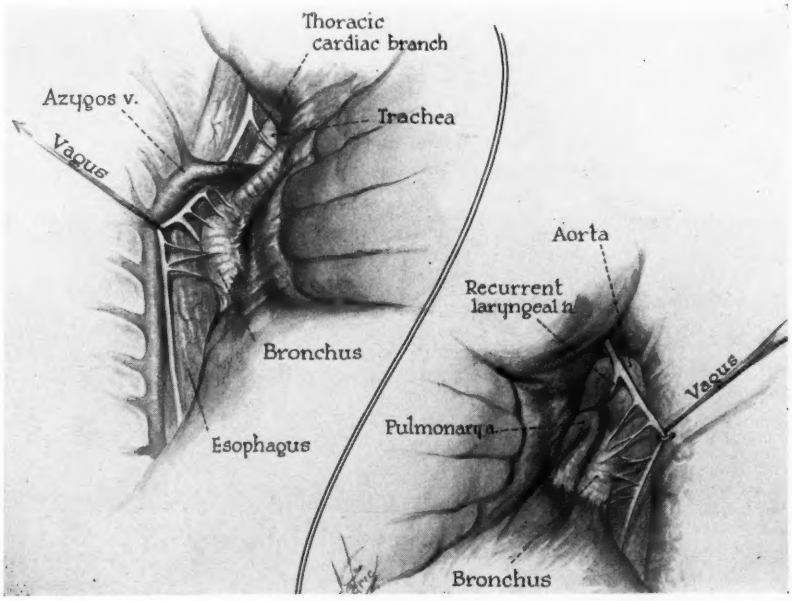

Fig. 3.—Cardiac catheterization pressure tracing.

## RESULTS

In all dogs, division of the vagal branches to each lung resulted in bilateral absence of the Hering-Breuer reflex. It is assumed, then, that in all animals a complete pulmonary parasympathetic denervation was produced. Fluoroscopic and x-ray examination at the time of the final cardiac catheterization confirmed complete re-expansion and aeration of both lungs. In nine of the ten dogs studied, there was an appreciable fall in pulmonary artery pressure following pulmonary parasympathectomy (Fig. 5). The drop in pressure varied from 31 per cent to 71 per cent, with an average decrease of 46.5 per cent. Pressures in the right ventricle showed a corresponding change (Table I). Cardiac output, as reflected in systemic blood pressure, showed no change immediately following the denervation.

DISCUSSION

In the literature there are many confusing statements concerning the regulation of the pulmonary circulation by nervous mechanisms. Wiggers[5] states that vasomotor nerves are present to the lesser circulation, with vasoconstrictor impulses passing over the sympathetic pathways. He believes that evidence as to the course or even the existence of vasodilator fibers remains less certain, and rather confusing. Cournand[6] states that there is little conclusive evidence for vasomotor control of the pulmonary circulation in normal man. Drinker[7] thinks that there is no reason as yet to believe that the pulmonary capillaries behave like those in the systemic circulation. He doubts the same type of parasympathetic and sympathetic control, which would be acting on the bronchial arteries, since they are systemic in origin.




*A.* *B.*

Fig. 4.—Vagus branches to right (*A*) and left (*B*) lungs.

Zimmerman[8] believes that there is a direct neurogenic control of the pulmonary circulation. He found that in man, adrenalin injection, which he assumed to mediate sympathetic vasoconstriction, resulted in an increased pulmonary artery pressure. Aminophylline resulted in a fall in pulmonary artery pressure, assumed to be due to parasympathetic stimulation and resultant pulmonary vascular dilatation. These drugs have manifold actions, however, including their effect on cardiac output. It is therefore perhaps unwarranted to assume that any effect on pulmonary artery pressure resulting from their use is due solely to their action on the pulmonary vascular tree.

TABLE I. PULMONARY ARTERIAL AND RIGHT VENTRICULAR PRESSURES (MM. HG) BEFORE AND AFTER BILATERAL PULMONARY PARASYMPATHETIC DENERVATION

| | PULMONARY ARTERY | | | RIGHT VENTRICLE | | |
|---|---|---|---|---|---|---|
| DOG NO. | PREOP. | P.O. | % SYSTOLIC CHANGE | PREOP. | P.O. | % SYSTOLIC CHANGE |
| B 1 | 21/9 | 37/21 | +43 | 20/2 | 31/0 | +35.5 |
| 2 | 40/23 | 20/7.5 | –50 | 43/9 | 23/0 | –46.5 |
| 3 | 25/2.5 | 16/8 | –36 | 25/0 | 16/0 | –36 |
| 4 | 34/18 | 10/6 | –71 | 35/0 | 10/0 | –71 |
| 5 | 18/5 | 12/4 | –33 | 25/–3 | 11.5/0 | –54 |
| 6 | 21/5 | 14.5/6 | –31 | 24/–8 | 14/0 | –42 |
| 7 | 16/11 | 8.5/3.5 | –47 | 18/0 | 9/0 | –50 |
| 8 | 23/8 | 13/5 | –43.5 | 28/0 | 12/0 | –57 |
| 9 | 30/5 | 19/11 | –37 | 27/–4 | 21/0 | –22 |
| 10 | 20/5 | 6/3 | –70 | 23/–6 | 6/0 | –74 |
| | | av. fall = 46.5% | | | av. fall = 50.3% | |

Dresdale and his associates,[9] in a study of patients with so-called primary pulmonary hypertension, find that Priscoline produces a transient lowering of the pulmonary artery pressure. Since this agent is sympatholytic, they conclude that pulmonary hypertension is perhaps related to isolated sympathetic overactivity, and broach the question of thoracic sympathectomy in its treatment. The same objection may be raised to this conclusion, since Priscoline is a drug acting throughout the body, and not only on the pulmonary vessels. The results of our study, moreover, if confirmed by further repeated observations, would indicate that more attention should be directed toward the parasympathetic innervation.

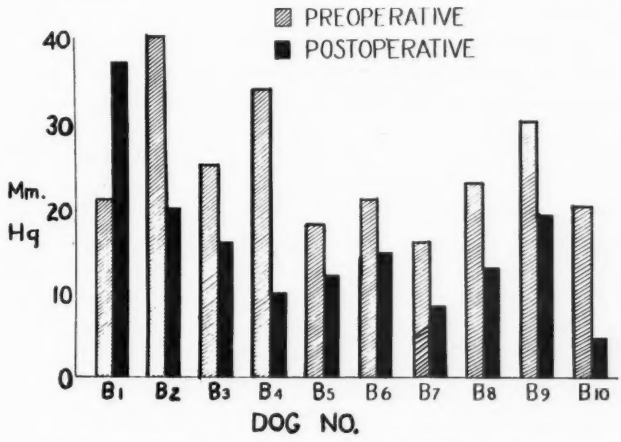



Fig. 5.—Effect of parasympathetic denervation of the lung on pulmonary artery pressure.

Rodbard[10] advances the theory that the bronchiolar muscular tone is of prime importance in regulating the pulmonary circulation, because of its effect on intra-alveolar pressure. Intra-alveolar pressure falls when the bronchioles dilate during inspiration and rises when the bronchioles constrict during expiration. Changes in intra-alveolar pressure are reflected in an increased

pulmonary artery pressure during expiration, and a decreased pressure during inspiration. Adrenergic influences dilate the bronchioles, which should result in a decreased pulmonary artery pressure. Vagotonic influences cause bronchiolar constriction, and consequently should increase pulmonary artery pressure. Vagus denervation of the lung would therefore be expected to allow an unopposed bronchiolar dilating action of normal sympathetic tone, resulting in a lowering of pulmonary artery pressure. We have demonstrated a decrease in pulmonary artery pressure following pulmonary parasympathetic denervation. Whether the mechanism of this effect, however, is directly on the vessels or indirectly on the bronchioles is not clear.

Blades and his co-workers[11] mentioned a study of the pulmonary artery pressure in dogs before and after their operation of bilateral pulmonary plexus resection. A decrease in pressure in one dog was cited after the operation. This procedure was intended to produce both a parasympathetic and sympathetic denervation of the lung, however. Therefore the part played by either parasympathetic or sympathetic activity in controlling the pulmonary vascular bed is difficult to determine in their experiment.

Parasympathetic denervation of the lung has been recommended in the past for various types of pulmonary pathology. Klassen and associates[12, 13] have utilized it for palliation in inoperable carcinoma of the lung and as treatment for intractable asthma. They state that each side of the bronchial tree receives nerve fibers from the contralateral vagus and sympathetic nerves. This is not borne out by our findings, for in all dogs studied, homolateral absence of Hering-Breuer reflex was demonstrated following unilateral parasympathetic denervation. This would indicate that vagus innervation of the lung is unilateral. The work of Larsell and Burget[14] substantiates this, for they demonstrated absence of cough on stimulation of intrapulmonary bronchi after ipsilateral section of the vagus nerve.

Abbott with his co-workers[15] tested complete pulmonary autonomic denervation, either alone or as an adjunctive procedure, in a variety of conditions, such as asthma, pulmonary emphysema, and bronchiectasis. Blades and his associates[11] reported on complete autonomic pulmonary denervation in the treatment of intractable asthma. In all these discussions, a complete parasympathetic denervation of the lung was assumed, but not proved. Judging from the magnitude of the dissections described, the denervations were complete. It would be valuable, however, to have objective proof of this, by testing for the presence or absence of the Hering-Breuer reflex postoperatively with the bronchospirometric technique described previously. Then, too, perhaps so extensive a dissection is not necessary to produce a total parasympathetic denervation. The absence of the Hering-Breuer reflex should enable the surgeon to determine the minimal division of nerve fibers needed to produce a total denervation effect.

## CONCLUSIONS

In the dog, complete parasympathetic denervation of both lungs was accomplished by dividing only the vagus branches to each lung. Completeness of the

denervation was proved by demonstrating the bilateral absence of the Hering-Breuer reflex postoperatively. A decrease in pulmonary artery pressure was observed as a result of this pulmonary parasympathetic denervation. This would indicate that the parasympathetic innervation of the lung has a significant role in the regulation of blood pressure in the lesser circulation. Whether this is a direct or indirect effect is not known.

## SUMMARY

1. A test for determining completeness of parasympathetic pulmonary denervation is described. This consists of determining the presence or absence of the Hering-Breuer reflex unilaterally during bronchospirometry.

2. Following pulmonary parasympathectomy, pulmonary artery pressure fell in nine of ten dogs studied, with an average decrease of 46.5 per cent.

3. The use of the test for complete parasympathetic denervation of the lung is discussed with reference to operative procedures designed to accomplish this result clinically.

The technical assistance of Miss Mary Marcy and Mr. William Kammerer is gratefully acknowledged.

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## DISCUSSION

DR. EDWARD J. BEATTIE, JR., Chicago.—I have enjoyed Dr. Kaunitz's discussion of this problem very much, and I was interested in his further work on it. Dr. Blades and I struggled with this same problem for several years and unfortunately even after that time could not come to a final definite conclusion. There is one question I would like to ask Dr. Kaunitz. Did he, or is he planning to, run any bilateral thoracotomy control experiments to contrast with this series? In dogs we found that the bilateral operation, in itself, had certain adverse effects.

One thing we did in trying to study the problem was to try to estimate the response of the lesser circulation to emboli after the lesser circulation had been denervated. Of course we were trying to produce complete denervation, getting both the parasympathetic and the sympathetic. I found that although in some animals there seemed to be some drop in pulmonary artery resting pressure after denervation, yet if we used embolization some months after denervation, the degree of hypertension produced in the experimental animals with the pulmonary artery denervated was just about as high as in the animals that had not been denervated, the bilateral thoracotomy controls. Pulmonary pressure after giving emboli could rise over 100 mm. of mercury systolic pressure in the pulmonary artery.

Another point that is worth emphasizing is that attempts to study the dynamics of the lesser circulation with drugs is very difficult, because it is difficult to know whether the drug is producing its effect on the left side of the circulation or the right side of the circulation. I know of no way that I could tell what the effect of the drug was, because of fall in pressure due to relaxation of the peripheral arterioles, change in left ventricular output, and so forth.

Dr. Blades and I hoped we were going to get the answer to this problem in some of our human patients in doing the asthma operation. After our struggles in the laboratory it seemed to me that we could get an answer to some of the problems by measuring the pulmonary artery pressures with a cardiac catheter in human patients in whom we were later going to denervate the lungs for asthma operations. Unfortunately, we started this project just about the time we stopped doing asthma operations, cortisone and ACTH came along, and our cardiac consultants had difficulty in getting the pressures, so I cannot give you the data. But I think that may be the way to get the answer if we start doing asthma operations again. I think that some of the problems are by no means solved, however.

DR. J. KARL POPPE, Portland.—This paper has been extremely interesting to me and I would like to report one case of Ayerza's disease or primary pulmonary hypertension in which I did a plexectomy. This patient, a 33-year-old man, came to me after having spent approximately nine months of almost complete hospitalization, being discharged for only periods of six or eight hours at a time before he returned in search of more oxygen to relieve precordial pain and dyspnea of which he complained. Based on Blades' report that the removal of the sympathetic and parasympathetic nerves on the left side would reduce the pulmonary artery pressure in dogs, that procedure was done according to the method described by Blades, of resecting all the nerve fibers around the bronchus, the pulmonary artery, and the two pulmonary veins.

This particular patient had that done three years ago. Before operation he had a pulmonary pressure of about three times normal level. Since that time he has had three subsequent cardiac catheterizations, once each year, and the pressure has been normal on each occasion. He was expected to require a contralateral nerve section on the right side but that has not seemed necessary. The only reason we were able to do these repeated catheterizations is because the man is still on total disability insurance from the fire department, although he is working every day selling insurance.

The only complicating element in this case is that an upper dorsal sympathectomy was done during the same operation on the left chest with removal of the second through the fifth sympathetic ganglion to ensure relief from the precordial pain. However, that should have had no effect on the pulmonary pressure.

DR. AARON HIMMELSTEIN, New York.—The control of the pulmonary circulation is an intriguing problem, particularly in investigation of the normal levels. If we stop to think how beautifully the correlation between ventilation and circulation is maintained in this low pressure system, and that very subtle changes in resistance in one small area of lung will tend to shift blood either into or away from that area of lung, I think we might pursue the problem of the control of pulmonary artery pressures, and more particularly of the control of local areas of resistance by less than complete denervation of both lungs. If we would attempt to denervate only one lung and then see if we can show that blood is

circulating in greater or lesser volume through that lung, as indicated by either rising or lowered oxygen consumption to that lung or, if possible, to a segment of it, we might have some idea of how the circulation is controlled, rather than by attempting only to measure gross pulmonary artery pressures. Studies under stress of exercise, or anoxia, or drugs might then be added.

With that in mind we have undertaken to denervate one lung in dogs by division and resuture of the bronchus to one lung. In the first group of dogs we have divided everything but the vessels and then stripped the vessels. That was done because the division and suture of the vessel might in itself cause some change in the flow through these vessels. When we studied a small group of these animals by bronchospirometry, and put stress on the system with anoxia (since we do know that anoxia in human beings and in animals does cause pulmonary hypertension by increase of resistance and, in severe anoxia, of flow) we were unable to show that in the preparations just described that there was any detectable shift in oxygen consumption, either normally or when stress was applied to one lung or both lungs, using low oxygen gas mixtures.

DR. MAX G. CARTER, New Haven.—All of us who have anything to do with cardiac catheterization realize how very complex this problem is, and I personally am very happy to know that Dr. Kaunitz is attacking it in this fundamental manner. I would like to ask him just two questions: Does he have any evidence that the lowering in pulmonary artery pressure is on a long-term basis? The second question, and I really wish Dr. Wright would discuss these problems and ask questions himself, is what changes if any may have been effected in the pulmonary volumina by this operation? I got the impression from the primary preoperative tracing showing the Hering-Breuer reflex, that when the reflex was instituted at the inspiratory level and the lung broke away on the opposite side and reassumed its respiratory rhythm, it did so at a higher level of residual air. It seems to me it would be of value to know, if it can be done without too much difficulty, whether or not any of the changes in pulmonary artery pressure are related to changes in pulmonary volumina, particularly residual volume.

DR. KAUNITZ (Closing).—I would like to thank the discussers very much for their interest in this subject. In answer to Dr. Beatty, we did not do controls on these dogs because the final studies were done anywhere from four to ten to twelve weeks after the second operation, at which time the dogs were running around the kennel, and we thought we had normal dogs except for the operations. As I mentioned, fluoroscopic and x-ray studies at the time of the final cardiac catheterization showed an apparently normal lung field.

We attempted to limit this denervation to one system and did not do a complete plexus resection in order to get at some of the answers. We thought that by removal of both sympathetic and parasympathetic nerves to a lung, little change would result because of the balancing effect of antagonistic denervations.

In answer to Dr. Carter, it is difficult to draw any conclusions from the one tracing you saw. Actually, if we let the dog breathe for awhile both lungs returned to their normal level of respiration, and I do not think there was any change in the residual volumes.

We merely wished to present the results of this little experiment, and we cannot, of course, draw any conclusions from it. There is much further work necessary in this field.

# FOURTEEN YEARS' EXPERIENCE WITH CARDIOPEXY IN THE TREATMENT OF CORONARY ARTERY DISEASE

SAMUEL A. THOMPSON, M.D., F.A.C.S.,* AND AARON PLACHTA, M.D.**
(BY INVITATION)
NEW YORK, N. Y.

CARDIOPEXY' is an operation used to increase the blood supply of the myocardium.[1] This method was developed and perfected by animal experimentation and adopted because it could overcome the effects of a sudden complete ligation of one of the coronary arteries, and the same ligation, without the operation preceding it, resulted in a mortality of 50 per cent. The operation thus appeared to be of value in decreasing the seriousness of a coronary closure.[2]

In our animal experiments, we found that the insertion of a nonabsorbable and irritating substance, namely, magnesium silicate powder (U.S.P. Talc), within the pericardial sac, produced a foreign body reaction which had several characteristics. First, there was a marked hyperemia of the myocardium with dilatation of pre-existing blood vessels and the formation of new blood vessels within the myocardium. Second, a foreign body granuloma was produced which involved the pericardium and superficial surface of the myocardium. Third, adhesive granulomatous pericarditis without constriction took place, and the myocardial blood supply was further enhanced by the anastomosis of the extracardiac vessels from the mediastinal structures with the myocardial vessels through the bridge of the granulomatous pericarditis. This acute inflammatory reaction terminated in a chronic, adhesive granulomatous pericarditis with extracardiac and intracardiac vascular anastomoses, which were known to persist for ten years; we believe the chronic lesion will remain active as long as the individual lives. Since the particles of the magnesium silicate powder are not absorbed and very little is removed by the lymphatics or phagocytes, the greater part of the powder remains fixed in the adherent tissues of the pericardium and myocardium and serves as a constant and continuous source of irritation, hyperemia, and stimulation in the formation of new extra- and intracardiac blood vessels.

The possibility has occurred to us, that the granulomatous tissue might eventually change into scar tissue and with the passage of time, become avascular and thus afford no collateral circulation. We do not believe this takes place, and our opinion is based on a study of material dealing with human beings which was collected over a period of fourteen years; the material consists of ten necropsies. The patients were both men and women; their ages ranged between 40 and 64 years. The survival of these patients following cardiopexy was from one day to ten years.[3]

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*Thoracic Surgical Service, New York Medical College.
**Department of Pathology, New York Medical College.

In the study of these hearts, done by Dr. Plachta, a new technique was used which will be reported in a later paper.[3] Visual dissection, a thorough x-ray study using a colored radiopaque material, and a serial section microscopic study was carried out of the myocardium, pericardium, lungs, and diaphragm.

The lesion was characterized by a hyperemia of the pericardium extending into the myocardium and out into the surrounding mediastinal structures. The vessels of the pericardium anastomosed freely with the vessels of the mediastinal structures, as well as with the intercoronary vessels. The striking features of the granulomatous pericarditis were the persistence of the hyperemia, the uniformity and stability of the anastomotic blood vessels, and the presence of the talc crystals. The adhesive pericarditis was movable and permitted adequate cardiac mobility. These features did not deviate within a ten-year period of time (Figs. 1, 2, and 3).

Occasionally the lesion which follows cardiopexy has been compared to and described as similar to the lesion seen in constrictive pericarditis. Such a comparison is erroneous and far from the actual facts. In constrictive pericarditis the pericardium may or may not be adherent, but it is usually thickened and avascular. When the pericardium is removed from the myocardium little or no bleeding occurs. However, following cardiopexy, the pericardium is always adherent, has never been found to constrict or impede the myocardium in any degree, and is excessively vascular and hyperemic. When the pericardium is separated from the myocardium it is done with great difficulty as no distinct line of cleavage can be developed and bleeding occurs from both pericardial and myocardial surfaces. This condition was found to exist not only in the animal experiments but also in one patient who was explored four and one-half years following a cardiopexy. The necropsy studies up to ten years after cardiopexy also show the lack of similarity between the two conditions. None of our postoperative patients have ever exhibited any of the cardinal signs of constriction such as prominent neck veins, hepatomegaly and ascites, hypotension and increased venous pressure, and fluoroscopically fixed cardia.

During the past few years we have severely limited the indications for operation and accepted only those patients who were more or less terminal cases of coronary disease with a marked degree of disability.[2] In view of the results which have been obtained we now believe that with more liberal indications, the operation can be successfully applied to a much larger group of patients. Since the rationale of the operation is to produce a myocardial hyperemia, it could be used to counteract the effects of those lesions which produce myocardial ischemia. The majority of lesions producing ischemia fall into three groups, namely, coronary artery disease, hypertension, and rheumatic disease. Together they are responsible for about three-fourths of all cardiovascular deaths.

The indications for cardiopexy in coronary artery disease are prophylactic, actual, and palliative. A young individual with coronary disease, with

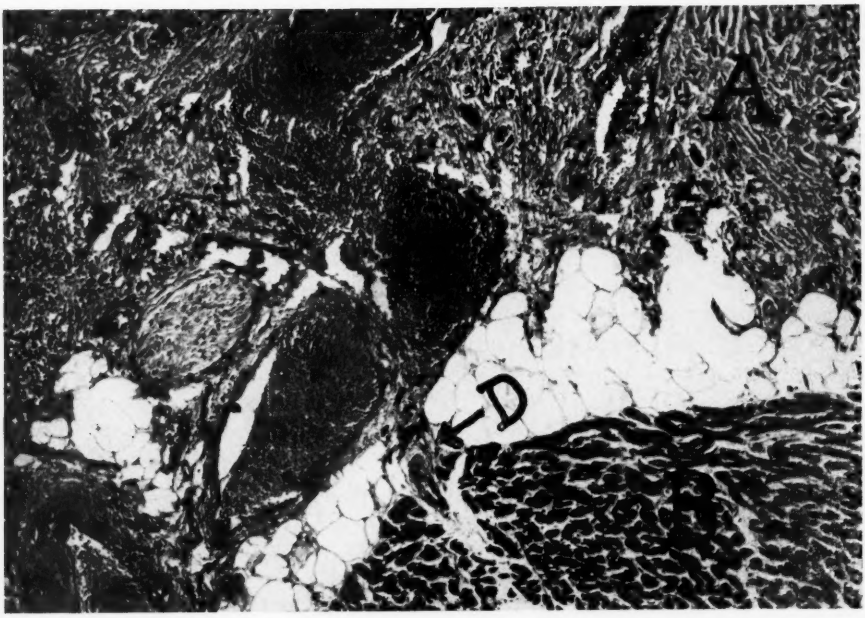


Fig. 1.—Microphotograph (×160) ten years after cardiopexy. The granulomatous pericarditis is still active and vascular and contains the particles of powder which are seen best with a Polaroid filter (Fig. 2). *A*, The zone of granulomatous tissue containing numerous blood vessels. *B*, The myocardium. *C*, A large blood vessel traversing the granulomatous area and connecting with a myocardial blood vessel at *D*.

Fig. 2.—The same microphotograph as shown in Fig. 1, but with a Polaroid filter added. The magnesium silicate (talc) crystals can still be seen scattered through the granulomatous tissue.

no hypertension, without valvular involvement, and without a previous infarction is an example of a prophylactic indication. An older individual with marked angina, with one or more previous infarctions, with hypertension or valvular involvement, with beginning congestive failure, and more or less completely incapacitated is an example of a palliative indication. Between these two examples, probably lies the greatest usefulness of cardiopexy in coronary artery disease.

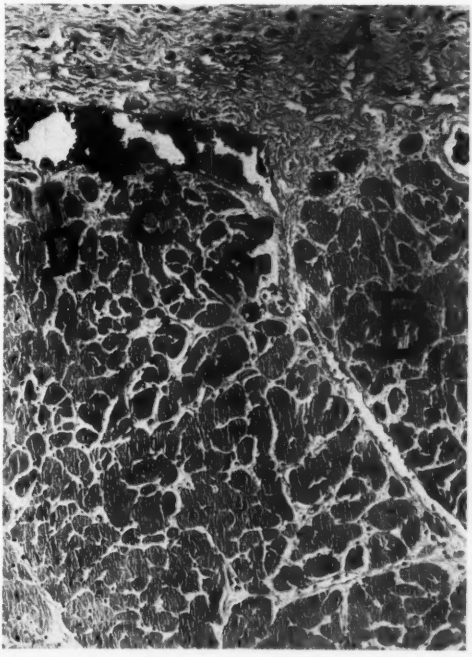

Fig. 3.—Photomicrograph (×70) seven and one-half years after cardiopexy. The granulomatous tissue contains numerous blood vessels and talc crystals. There are several large blood vessels between the myocardium and the granulomatous tissue connecting with myocardial blood vessels. *A*, Granulomatous pericarditis. *B*, Myocardium. *C*, Large blood vessels connecting at two places with myocardial blood vessels at *D* and *E*.

It is a matter of record that the majority of hypertensive patients die a cardiac death.[4] Some of these patients die from congestive failure and in many of these instances, myocardial ischemia is the predominating factor. Many of these patients with hypertensive disease develop a marked angina which may be indicative of a relative coronary insufficiency rather than actual coronary disease. In 500 hypertensive patients operated upon by Hinton and reported by Thorp,[5] myocardial ischemia, as evidenced by angina and previous infarctions, was the chief complaint before the operation in more than 30 per cent of the patients. Hypertension has been reported by many groups to exist prior to myocardial infarction in from 23 per cent to 73 per cent of the cases.[6] Still in other cases of hypertensive disease, with

no angina, with no evidence of congestive failure, but with a marked enlargement of the heart and the electrocardiogram demonstrating a definite left axis deviation and a positive Master two-step test, the finding of these signs indicates a myocardial ischemia. Therefore the indications for cardiopexy in hypertensive disease are: when angina is present, when there has been a previous infarction, when beginning heart failure is evident, and when there is no congestive failure and no angina but the heart is enlarged and the electrocardiogram shows a marked enlargement of the left ventricle with a positive Master two-step test.

The clinical features or symptoms in chronic rheumatic valvular disease are due as much to the state of the myocardium as they are due to the valvular involvement. Severe valvular involvement or even multiple valvular involvement is compatible with life so long as the heart muscle remains relatively strong. Rheumatic disease produces three principal changes in the heart: changes in the valves, changes in the coronary arteries, and changes in the myocardium. The valvular changes result in stenosis or regurgitation or a combination of the two. The myocardial changes are a low-grade inflammation resulting in fibrosis and ischemia. Rheumatic fever regularly produces changes in the coronary arteries, inflammatory or fibrotic lesions or both are constantly observed, and myocardial damage is associated with these arterial lesions.[7] The decision for or against the surgical treatment of chronic valvular disease requires a careful estimation of the degree of valvular dysfunction as well as the myocardial dysfunction. The possibility of treating myocardial dysfunction as a primary object in chronic valvular disease has been completely overlooked until recently. A few years ago Gorelik[8] became convinced that many of the symptoms observed in chronic valvular diseases were due more to myocardial ischemia than they were to the valvular disorder and he was the first to use cardiopexy as a treatment in chronic rheumatic valvular disease.

Whenever possible in valvular stenosis a splitting or cutting of the valve commissure should be done. However, there are times when such a procedure may not be indicated because of marked myocardial damage, and a damaged left ventricle may be unable to carry the increased load following the relief of the obstruction.[9] Marked regurgitation associated with the mitral stenosis is also a contraindication for commissurotomy, as is prolonged pulmonary hypertension with the development of pulmonary arteriosclerosis. Associated valve lesions such as aortic stenosis, as well as prolonged passive congestion due to right heart failure with marked liver changes, make mitral surgery impractical. It is at such a time that the surgical treatment can best be directed toward revascularization of the heart and restoration of myocardial function. Because cardiopexy produces a myocardial hyperemia, it aids in the restoration of the myocardial function and is indicated in those conditions described previously where commissurotomy is not suitable. In some of these patients who have had cardiopexy, the improvement has been so marked that the patients later became satisfactory candidates for commissurotomy.

The contraindications would include those systemic and cardiac conditions where the risk is quite evidently too great for any type of operative procedure such as advanced renal and hepatic disease and extreme debilitation. A recent myocardial infarction is a definite contraindication and remains so until such time as the infarcted area has become well healed and we have arbitrarily set a minimum time of three months. Marked and intractable congestive failure, where cyanosis is present at rest, is also a contraindication.

The operation has been fully described in previous articles[1]; I will not now describe it more than to say that it consists of removing a portion of the fifth costal cartilage on the left side of the chest. At this site the pleura is not entered. The pericardial sac is opened, the pericardial fluid is aspirated as completely as possible and from 2 to 4 dr. of dry magnesium silicate powder is spread widely over the surface of the myocardium. The tissues are then closed in anatomic layers without drainage. It is a simple operation and requires about thirty minutes for its performance.

We have recently made a fourteen-year follow-up study of our patients who have had a cardiopexy.[10] In order to determine fully the effects of the operation, no patient has been included in this series who has been operated upon during the past twelve months. The total number of operations was fifty-seven. Deaths attributed to the operation and all hospital deaths after the operation numbered seven, giving an operative and hospital mortality of slightly more than 12 per cent. Thirty-three of the patients, or 66 per cent, are living at the present time.

Of the remaining fifty patients, who have been followed up to the present time, or the time of their death, thirty-seven were men and thirteen were women. This is a ratio of slightly less than three to one. The youngest patient was a woman 35 years old, and the oldest was a woman 68 years of age. The average age of the entire group was 51 years, and the majority of patients were in the sixth decade. The shortest duration of symptoms before the operation was three months and the longest was fifteen years, giving an average of three and one-half years. There is a sharp difference, however, in the duration of symptoms of the patients who are still living and in those who have died. The living patients averaged symptoms for two and three-quarter years while the patients who have died averaged symptoms for four and one-half years before operation.

In thirty-seven patients, angina occurred as the first symptom, and coronary occlusion was the first symptom in thirteen. Three of the patients had congestive failure, and seven had hypertensive disease.

The shortest length of life after the operation was two months and the longest is now over fourteen years, with an average of five years plus. However, thirty-three of the patients are still living so this average is subject to a change as time goes on.

Of the seventeen patients who were followed up to the time of their death, the average duration of symptoms before operation was four and one-half years and the average life span after operation was five years. Thus

the span of life of these patients from the first symptom was nine and one-half years. This compares very favorably with the span of life of the average coronary patient who is not operated upon. Statistics upon these patients vary with each group reported, but averaging the groups gives a life span of four to five years from the onset of the first symptom. Factors such as cardiac enlargement, hypertension, infarction, congestive failure, and conduction defects in coronary disease indicate a much less favorable prognosis; some of our patients had all of these conditions, and all had some of the conditions.

Our group of patients is small and no definite conclusions should be drawn from a small group. We nevertheless believe that the span of life for these patients has been markedly increased by the operation for two reasons. First, the average length of life for these patients was nine and one-half years compared to four and one-half for the average nonoperated coronary patient. Second, the large majority of these operated patients were terminal cases, completely incapacitated, having been through one or more occlusions and very few of them were good surgical risks or could be presumed to continue life for any length of time. They had already lived for four and one-half years and were thus at the end of the average life span for coronary patients, yet they continued to live after the operation for an additional average of five years.

There are four tests which we use to determine the postoperative benefits. First, the decrease in the amount of anginal pain. Second, the increase in the exercise tolerance. Third, the improved ability to attend to their daily needs. Fourth, a return to their former, or some gainful, occupation. Using these four tests as a guide, we have divided the patients into three groups: The first group having less than 50 per cent improvement we classify as poor results. The second group having from 50 to 75 per cent improvement we classify as moderate results. The third group having more than 75 per cent improvement we classify as having marked results.

Of the fifty patients followed, five or ten per cent have received less than 50 per cent improvement. The remaining forty-five patients, or 90 per cent of the group, have received more than 50 per cent improvement. Twenty of these patients, or 40 per cent of the group, have received more than 75 per cent improvement as measured by the four tests and are classed as markedly improved.

The postoperative electrocardiographic changes are usually confined to the immediate postoperative period of several weeks.[1, 2] The changes are those characteristic of acute pericardial reaction and consist of an elevation of the RS-T segment with a downward concavity of the S-T segment. The changes revert to the preoperative pattern after several weeks. None of the patients in this series had a normal electrocardiogram before the operation, nor did the electrocardiogram return to normal after the operation. The electrocardiographic recovery does not appear to be as important a factor in the prognosis as does the clinical recovery.[11]

Objective evidence of the mediastinitis is obtained by means of serial x-ray films. The characteristic changes are a widening and increased density of the mediastinal shadow together with some increased markings in both lower lobes of the lungs. These changes revert to normal in about two or three weeks.

## CONCLUSIONS

For a group of patients who were medical failures, this operation has produced most satisfactory results. It should be emphasized that almost all of the patients were terminal cardiac cases and more or less completely incapacitated. Few of them were satisfactory as surgical risks. As a result of the operation we were able to rehabilitate these patients so that 90 per cent of them were improved more than 50 per cent, and 40 per cent are more than 75 per cent improved.

In addition to their physical improvement, the patients who later on died, lived an average length of life after the operation of five years, giving them an average life span of nine and one-half years from the onset of the first symptoms. We do not believe that these patients would have survived this length of time without the operation.

I am grateful to Dr. Milton J. Raisbeck, Department of Cardiology of the New York Medical College, for his generous cooperation and for the selection and medical management of most of these patients before, during, and after the operation.

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## DISCUSSION

DR. H. BRODIE STEPHENS, San Francisco.—I wonder if Dr. Thompson will tell us if any of the patients that died following operation came to necropsy and, if so, if any of them died from coronary occlusion.

DR. GABRIEL SELEY, New York.—I have followed Dr. Thompson's work with a great deal of interest, and I would like to ask him at this time whether or not it would

be feasible to perform this procedure in a much simpler manner. In other words, since the object of the operation is to aspirate pericardial fluid and introduce a talc powder, could this not be done through a large bore aspirating needle, using a powder insufflator or some other mechanism.

DR. THOMPSON (Closing).—I would like to thank Dr. Stephens and Dr. Seley. These patients have had subsequent coronary attacks and subsequent closures, following cardiopexy. They have not suffered too severely from those occlusions. They have died from a variety of causes. We have never, in any of the ten necropsies which we were able to get, found any fresh infarctions. We suppose that two of the patients who apparently died from fibrillation, would probably have had infarctions if they had survived the attack, but there was no evidence of acute infarction at the time of necropsy.

About simplification of the operation I would like to say that in the animal laboratory we found it impossible to produce the same results if we tried to dilute the powder with any type of vehicle. We tried various salines and other carriers, and we found that the tendency is for the powder to wash down in the dependent part of the pericardial sac, and when this occurs we get incomplete pericardial adhesions and a very limited area of granulomatous tissue formation. We like to have the adhesions and granulomatous tissue completely surround the heart. It is very difficult to insert a trocar in the pericardial sac; it is sometimes difficult even to pick up the pericardial sac with hemostats, because it is stretched very tightly over the heart like the head of a drum. I think the danger of trying to simplify this further would outweigh the actual simplicity of the operation.

# CARDIAC SURGERY UNDER HYPOTHERMIA

CHARLES P. BAILEY, M.D., BRIAN A. COOKSON, M.B., CH.B.(EDIN.) (BY INVITATION), DANIEL F. DOWNING, M.D. (BY INVITATION), AND WILFORD B. NEPTUNE, M.D. (BY INVITATION)
PHILADELPHIA, PA.

HYPOTHERMIA may be defined as a physical state in which the body temperature is below the normal range. Artificial hypothermia, as it will be discussed here, refers to the selective lowering of the temperature by physical means. For the purposes of cardiac surgery we may consider that the proper state is achieved below 90° F. (32.2° C.), preferably between 74° and 80° F. (23.3° C. and 26.6° C.). Temperatures appreciably below 70° F. (21.1° C.), while used experimentally, tend to depress the vigor of cardiac contractions and function to such a low level that the damaged human myocardium associated with serious anatomic cardiac defects probably could not accept the ordeal and subsequently recover full function.

The value of low body temperature in cardiac surgery is twofold: 1. At low temperatures the tissue demand for oxygen is significantly depressed. This varies almost directly with the degree of cooling. The circulation, therefore, may be greatly slowed or even completely interrupted for a relatively long period of time without evidence of damage to brain, kidneys, or other viscera. 2. Myocardial activity is depressed. Its demands for oxygen are so reduced that a blood supply which would lead to ischemia and damage at normal temperatures is well tolerated. It is probable that for each individual there is a critical temperature level below which function may be depressed to an irreversible degree. It is evident that the infantile heart is much better able to tolerate very low temperatures and to recover from them than is the adult heart.

The idea of possible clinical application of hypothermia is not new. There is a large body of medical literature covering the experimental and clinical use of hypothermia. The work of Fay[1] and Talbot[2] in the clinical field is fundamental. McQuiston[3] and Potts[4] have already reported its use in clinical cardiac surgery.

In the laboratory the possibilities of hypothermia have been rather fully explored.[5, 6] Following the lead of Bigelow and his associates,[7-9] we, too, have undertaken extensive investigations in the field of experimental cardiac surgery.[10, 11] It was found possible to lower the body temperature of dogs to such a degree that the venae cavae could be clamped and the right heart opened for prolonged periods with the survival of the animals and with no

From the Divisions of Surgery and Pediatrics, Hahnemann Medical College and Hospital and the C. P. Bailey Thoracic Clinic.

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subsequent evidence of organ damage (Fig. 1). Opening of the left side of the heart, on the other hand, was frequently attended by the development of coronary, cerebral, or systemic arterial air embolism. It was realized that this risk was inherent in the application of open surgical techniques to the left side of the heart and not really to the hypothermia itself. Attempts to use the so-called "mechanical heart" to permit open surgery of the left atrium or left ventricle are similarly attended by a high incidence of arterial air embolism.

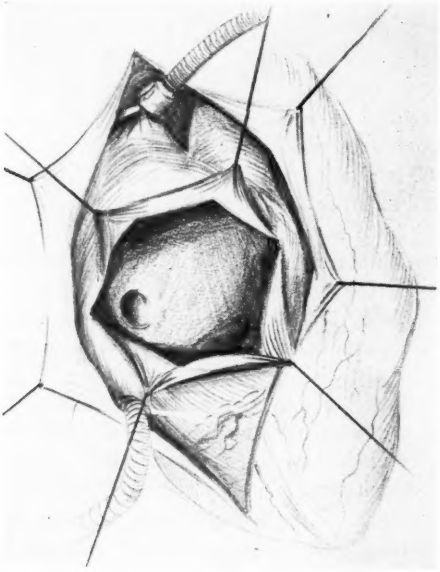


Fig. 1.—Wide opening of right atrial chamber after intrapericardial tourniquet compression of both venae cavae for intracardiac surgery under direct vision. This is feasible under hypothermia.

The use of arterial transfusions to maintain a high pressure in the aortic arch was found to reduce the incidence of such air embolism significantly, apparently by keeping the aortic valves closed while the left ventricle was open to the air (Fig. 2). In this connection it is important to point out that citrated blood so used appears to be quite toxic to the heart, rapidly producing ventricular fibrillation. Red cells suspended in Gelatin-Ringer solution* appear to have no such deleterious effect.[12] It may be found desirable in the future to use only such nontoxic suspensions of red cells in routine arterial transfusions. Probably some unexplained deaths occurring in the clinical use of arterial transfusion may be attributed to the direct entrance of citrated blood into the coronary arteries.

It also appears that the use of arterial transfusions significantly prolongs the period at any given body temperature during which the circulation may

*Modified fluid gelatin No. 8 generously supplied free by Dr. Tourtelotte of the Knox Gelatin Company, Camden, N. J.

be completely clamped off, by perfusing the brain, the coronaries, and other parts of the circulation. Thus, while twelve minutes has been considered the maximum safe time for clamping the venae cavae in dogs at 76° F. (24.4° C.), twenty minutes is perfectly safe with a rapid arterial transfusion.[12]

We have attempted to translate these experimental observations in terms of human beings. Our first problem was the selection of suitable individuals for surgery under hypothermia.

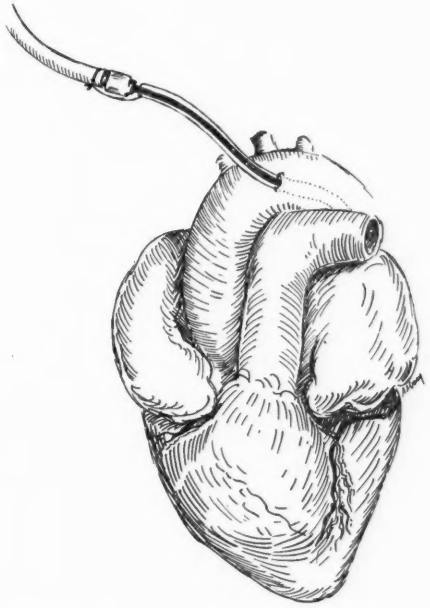


Fig. 2.—Direct intra-aortic transfusion of red blood cells suspended in Gelatin-Ringer solution. This perfusion of the coronaries and cerebral vessels permits prolongation of the time of circulatory interruption at any temperature level. Also the fluid pressure closes the aortic valve lessening the risk of air embolism when the left ventricle is opened.

At the present time there exist many techniques of closed or digital intracardiac surgery,[13-21] which are satisfactory for the moment. However, there is a strong feeling that several of the operations could be considerably improved upon if they could be performed by an open technique under direct vision. For instance, catheterization studies some time after operative relief of the obstruction in isolated pulmonic stenosis (either valvular or infundibular) by the Brock technique nearly always show a residual pressure differential between the right ventricle and the pulmonary artery. While great clinical improvement has usually been obtained by this procedure, it is obvious that the obstruction has been incompletely relieved. Undoubtedly, a more complete relief could be obtained by an open technique.

Such an open technique might be feasible by the use of a "heart-lung" apparatus, but could be equally well accomplished by the simpler method of

hypothermia. Since the "heart-lung" is not yet sufficiently perfected for clinical use, it would seem logical to use hypothermia for this purpose.

While hypothermia does permit the performance of such procedures, in its present stage of imperfection, many of the older techniques are still preferable. As the imperfections of hypothermia and methods of managing it are progressively remedied, there will probably be a gradual switch-over to the new techniques of operation under direct vision. In this earliest phase of the development of hypothermia we can justifiably apply it only to problems for which there is no other answer or as an adjunct to orthodox surgical techniques.

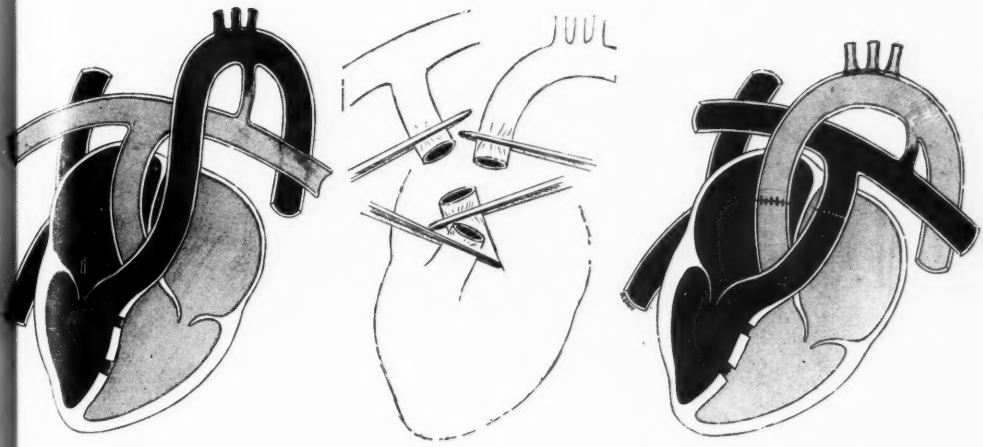
While we early realized the danger of opening the right atrium in patients with a large interatrial communication, we were originally of the opinion that the very primitive low defect of the interatrial septum, known as persistent ostium primum, could be corrected only by an open technique. We now realize that a slight modification of the technique of atrio-septo-pexy[19] originally described for the surgical closure of defects of the septum secundum (effective in thirteen of fifteen such patients operated on by us to date) is eminently satisfactory for the complete obliteration of the persistent ostium primum.

The first patient (H. D.) chosen for the open technique had a very large persistent ostium primum. The right atrium was widely opened on Aug. 29, 1952, and the defect was closed by direct suturing. However, air embolism to the coronaries caused the onset of ventricular fibrillation which proved irreversible.

Since that time hypothermia has been employed in twelve additional cases of serious heart disease; an open technique was employed in three, while a closed technique was used in the others. Actually, three classified as closed were patients with transposition of the great arteries which were treated by division between clamps and cross-anastomosis (Fig. 3, *A, B, C,* and *D*).

The results in our entire series are summarized in Tables I, II, and III. It will be evident that the over-all surgical mortality has been prohibitive (69.2 per cent). The possible extenuating factors are the severity of the lesions (five congenital transpositions) and the condition of the patients so operated. Among the surviving patients it was felt that B. L. and S. G. were so ill that they could not have survived orthodox surgery (Brock infundibulectomy) except with the help of hypothermia. M. A. F. certainly could not have had her interventricular septal defect corrected except by open surgery under hypothermia. J. S. probably would have done equally well with a standard atrio-septo-pexy performed at normal body temperature. We feel that K. C., one of the patients treated by division and reanastomosis of the transposed aorta and pulmonary artery, undoubtedly would have lived and done well had he not developed a cardiac arrest during a postoperative bronchoscopy for retained secretions (thirty hours later).

However, the operative death of two similarly treated patients with transposition included in this series has convinced us that this particular surgical approach is basically unsound since the coronary arteries nearly always arise



*A.* *B.* *C.*

*D.*

Fig. 3.—*A*, Case of K. C. Schematic diagram of his circulation. *B*, Division of both great arteries between clamps. *C*, Circulatory arrangement after crossed reanastomosis in K. C. *D*, Autopsy appearance of great vessels in K. C. Note the considerable discrepancy in the caliber of the vessels.

TABLE I

| | PT. | AGE | REMARKS | OP. DATE | LOWEST RECTAL TEMP. | OPERATIVE PROCEDURE | TECHNIQUE | INTERRUPTION OF CIRCULATION | RESULT |
|---|---|---|---|---|---|---|---|---|---|
| Atrial septal defect | H. D. | 30 yr. | Persistent ostium primum | 8/29/52 | 81° F. | Suture-repair defect | Open | 6 min. | Died |
| | I. D. | 27 yr. | Persistent ostium primum | 11/10/52 | 80° F. | Atrio-septo-pexy | Closed | 0 | Died |
| | J. S. | 11 yr. | Central defect | 9/19/52 | 88° F. | Atrio-septo-pexy | Closed | 5 min. | Living |
| Tetrology of Fallot | D. L. | 15 mo. | Extremely ill | 11/15/52 | 76° F. | Resection infundibular obstruction | Open | 4 min. | Died |
| | S. G. | 12 mo. | Extremely ill | 10/ 3/52 | 80° F. | Brock | Closed | 0 | Living |
| Ventricular septal defect | M. F. | 15 yr. | High defect 1½ × 1 cm. | 3/13/52 | 76° F. | Suture-repair defect | Open | 6½ min. | Living |
| Taussig-Bing | B. L. | 2½ yr. | Valvular pulmonic stenosis | 11/22/52 | 72° F. | Brock | Closed | 0 | Living |

TABLE II

| | PT. | AGE | REMARKS | OP. DATE | LOWEST RECTAL TEMP. | OPERATIVE PROCEDURE | TECHNIQUE | INTERRUPTION OF CIRCULATION | RESULT |
|---|---|---|---|---|---|---|---|---|---|
| Transposition of great vessels | K. C. | 7 mo. | All coronaries arose from right ventricular vessel | 11/10/52 | 71° F. | Switch-over anastomosis | Closed | 22 min. | Died 30 hr. later |
| | G. N. | 3½ mo. | | 3/ 6/53 | 72° F. | Switch-over anastomosis | Closed | 20 min. | Died |
| | C. R. | 11 da. | | 12/24/52 | 68° F. | Switch-over anastomosis | Closed | 23 min. | Died |
| | E. K. | 10 mo. | | 11/ 7/52 | 78° F. | Atrial septal defect created | Open | 5 min. | Died |
| Aortic insufficiency | T. V. | 33 yr. | Rheumatic | 1/20/53 | 88° F. | Exploration | Closed | 0 | Died |
| Mitral insufficiency | N. S. | 31 yr. | Rheumatic | 9/29/52 | 78° F. | Mitral commissurotomy and commissurorrhaphy | Closed | 0 | Died |

TABLE III

| | |
|---|---|
| *Survived* | |
| J. S. —closed | Atrial septal defect |
| S. G. —closed | Brock type infundibulectomy |
| B. L. —closed | Brock type pulmonary valvulotomy |
| M. F.—open | Ventricular septal defect |
| *Causes of Death* | |
| Air embolism | 2 (both open technique) |
| Myocardial depression | 3 |
| Cardiac arrest | 3 |
| Vago-vagal reflex | 1 (bronchoscopy) |

from the right ventricular vessel. Only cases with a large interventricular septal defect such as K. C. can maintain a sufficiently high pulmonary hypertension after the reanastomosis to permit sufficient coronary filling for continued cardiac function.

## CASE REPORTS

CASE 1.—H. D. was a 30-year-old white woman who had had cardiac catheterization studies done prior to admission. A diagnosis of atrial septal defect had been made. Previous exploration had revealed a very large persistent ostium primum which was then believed not amenable to atrio-septo-pexy. On Aug. 29, 1952, under hypothermia at 81° F. (27.2° C.), direct suturing was done by open technique. The circulation was occluded six minutes. Ventricular fibrillation developed at the completion of the repair and the patient could not be resuscitated. Air bubbles in the coronary arteries indicated the etiology of the fibrillation.

CASE 2.—I. D., a 27-year-old white woman, was found to have an interatrial defect on cardiac catheterization, with evidence of an interventricular defect also. ECG showed incipient right bundle branch block. On Nov. 10, 1952, under hypothermia at 80° F. (26.6° C.) atrio-septo-pexy by a closed technique for a persistent ostium primum was carried out. After thoracotomy the patient had to be restored from two episodes of ventricular fibrillation before atrio-septo-pexy was started. A third episode of ventricular fibrillation occurred during atrio-septo-pexy, and a fourth episode during closure of the chest proved fatal. It was felt that hypothermic depression of the myocardium was responsible for the death.

CASE 3.—J. S., an 11-year-old white girl, was admitted with a history of heart murmur since birth; recently she had experienced fatigue and syncope. Cardiac catheterization revealed an interatrial defect with a left-to-right shunt. On Sept. 19, 1952, under hypothermia at 88° F. (31.1° C.), the defect was closed by atrio-septo-pexy, and anomalous right pulmonary veins were transposed to the left atrium via the interatrial defect. The patient was discharged on the sixteenth postoperative day at which time she had no cardiac symptoms nor abnormal heart sounds. This patient probably could have been operated just as well at normal temperatures.

CASE 4.—D. L. was a 15-month-old white female infant. Cyanosis was first noted at 15 weeks of age; it progressively increased. Since age of 3 months, dyspnea had been progressive. Syncope developed while eating. Cardiac catheterization revealed findings consistent with the tetralogy of Fallot. This was confirmed at surgery on Nov. 15, 1952, under hypothermia at 76° F. (24.4° C.). Resection of the infundibular stenosis was carried out via the open technique permitting direct visualization through an incision of the right ventricle outflow tract. The patient developed cardiac arrest and then ventricular fibrillation from which she could not be restored. This operation should have been done by a closed technique. It was evident that air embolism to the coronary arteries had occurred.

CASE 5.—S. G., a 12-month-old white female infant, had a history of cyanosis from birth. Tachycardia had always been noted. She tired easily and more recently had become quite dyspneic. A diagnosis of the tetralogy of Fallot was made on clinical and roentgen findings as the infant's condition was thought to be too critical for cardiac catheterization. On Oct. 3, 1952, under hypothermia at 80° F. (26.6° C.), resection of the infundibular stenosis was carried out via closed technique. The result of the operation was exceedingly gratifying. It was thought that due to her extremely critical (practically terminal) condition, hypothermia might well have made possible her survival.

CASE 6.—M. F., a 15-year-old white girl, was admitted with a history of a heart murmur since birth but no signs nor symptoms of congestive failure. Cardiac catheterization revealed an interventricular defect. On March 13, 1953, under hypothermia at 76° F. (24.4° C.), the defect was sutured by an open technique utilizing an incision in the right ventricle. The patient developed ventricular fibrillation as the ventricular incision was being closed, but was restored to a normal rhythm by massage alone. Convalescence has been satisfactory to date. At surgery it was felt that the defect had been completely closed.

CASE 7.—B. L. was a 2½-year-old Negro girl with a history of cyanosis and cardiac murmur since birth. On admission she was markedly cyanotic, dyspneic, and demonstrated easy fatigability. Cardiac catheterization and angiography substantiated a diagnosis of transposition of the great vessels. The possibility of transposition of the aorta and levoposition of the pulmonary artery was considered. On Nov. 12, 1952, under hypothermia at 72° F. (22.2° C.), surgery was carried out. It was found that the patient had transposition of the aorta, high ventricular septal defect with levoposition of the pulmonary artery, and congenital fusion of the pulmonic cusps. Using the closed technique, pulmonary valvulotomy was carried out. Her postoperative course has been very satisfactory.

CASE 8.—K. C., a 7-month-old Negro boy, had a history of cyanosis since birth. A diagnosis of pulmonary stenosis and patent foramen ovale was made on incomplete cardiac catheterization. On Nov. 10, 1952, under hypothermia at 71° F. (21.6° C.), it was found that transposition of the great vessels existed. A switch-over anastomosis was done, the circulation being occluded for twenty-two minutes. Ventricular fibrillation occurred once, but a normal rhythm was restored. The patient was awake and crying three hours postoperatively. He developed cardiac arrest thirty hours postoperatively during a routine bronchoscopy for retained secretions. It was felt that he would have continued to do well if this accident had not occurred. The coronary arteries arose from the right ventricular vessel. A large ventricular septal defect existed.

CASE 9.—G. N., a 3½-month-old white boy, had had recurrent bouts of cyanosis and dyspnea since birth. Cardiac catheterization was attempted but discontinued because of the patient's poor condition. On clinical and roentgen examination, he was thought to have transposition of the great vessels. On March 6, 1953, a switch-over anastomosis was done under hypothermia at 72° F. (22.2° C.). The circulation was occluded for a total of twenty minutes. The heart action was extremely poor by the time the second anastomosis was completed. Heart action continued for two hours with the assistance of an electrical pacemaker. At post-mortem examination the coronary arteries were found to arise from the right ventricular vessel. There were a 0.7 cm. high septal defect and a patent ductus arteriosus. The foramen ovale was closed.

CASE 10.—C. R. was an 11-day-old white girl who had been cyanotic and dyspneic since birth. It was thought that the patient probably had transposition. On Dec. 24, 1952, under hypothermia at 72° F. (22.2° C.), transposition of the great vessels was found. A switch-over anastomosis was done, the circulation being occluded for a total of twenty-three minutes. Heart action became poor and finally ceased. The coronary arteries rose from the right ventricular vessel.

CASE 11.—E. K. was a 10-month-old white boy who had had a diagnosis of transposition of the great vessels made on cardiac catheterization prior to admission. He

had been cyanotic since birth. On Nov. 7, 1952, under hypothermia at 78° F. (25.5° C.), the diagnosis was confirmed. The coronary vessels came off the artery arising from the right ventricle. The circulation was interrupted for five minutes while a defect was made in the interatrial septum under open technique and direct visualization. The heart beats were never strong after the atrium was closed. After forty minutes of weak heart beats, ventricular fibrillation occurred and a normal sinus rhythm could not be restored.

CASE 12.—T. V. was a 33-year-old white man with a definite history of rheumatic fever at the age of 10 years and dyspnea and substernal pain for nine months. Preoperative work-up, including cardiac catheterization and brachial artery tracings led to a diagnosis of predominant aortic insufficiency, mild aortic stenosis, and possibly slight mitral stenosis. On Jan. 20, 1953, under hypothermia at 88° F. (31.1° C.), exploration of the aortic valve via the left ventricle was carried out prior to a planned attempt at direct repair of the valve. Ventricular fibrillation developed. Using a mechanical pump, blood was pumped from the left auricle into the left subclavian artery for a short period while massage was carried out. Normal sinus rhythm was restored for ten minutes. Ventricular fibrillation developed again, and when the pump was again used, the left ventricle filled with a large quantity of blood due to retrograde flow through the incompetent aortic valve. The ventricle became so hard it could not be adequately massaged. Normal sinus rhythm could not be restored.

CASE 13.—N. S. was a 31-year-old white woman with progressive dyspnea, orthopnea, and fatigability of three years' duration. Preliminary studies showed advanced mitral insufficiency. On Sept. 29, 1952, under hypothermia at 78° F. (25.5° C.), commissurorrhaphy (suturing the mitral leaflets together) was carried out. During the intracardiac surgery, cardiac arrest occurred followed by ventricular fibrillation which was resistant to all attempts at resuscitation. Examination of the left atrium after death revealed a clot to be present which was absent at the beginning of surgery. It was felt that the clot contributed to the onset of arrest and fibrillation. However, cardiac action had become extremely poor even before exploring the mitral valve.

## TECHNIQUE OF ADMINISTERING HYPOTHERMIA

Artificial lowering of the body temperature may be accomplished in many ways. Immersion in cold water, packing in cracked ice, a "deep-freeze" type of cold chamber, and a rubber blanket containing coils through which cold brine or other cool fluids may be circulated have been used. Certain drugs may be administered to depress the function of the thermal center and so facilitate lowering the body temperature. We are presently trying these drugs in experimental animals, but they have not yet been used on our patients.

We have had no experience with immersion (Fig. 4).

We have used cracked ice applied directly to the patient's entire body both for the clinical treatment of hyperpyrexia and as an adjunct in cooling patients whose body temperature was slow to descend with other methods of refrigeration. While messy, direct application of cracked ice is quite effective (Fig. 5).

The cold chamber, even when adequate air circulation is available, carries with it the threat of superficial frostbite or pressure gangrene because of the extreme coldness of the circulating air. Proper protection of the superficial portions of the body and the extremities militates against effective application of the cooling air and, hence, retards cooling (Fig. 6).

The blanket with circulating coils developed by Fay[1] is by far the most satisfactory cooling mechanism (Fig. 7).* By means of a compressor, or even an ordinary pump, cool liquid is circulated through the coils at any desired rate for rapid or slow cooling (Fig. 8).

The blanket is placed on the operating table and is closed about the patient with a zipper. When the desired temperature is reached, the blanket is opened but it is left in place under the patient while the operation is carried out (Figs. 9*A* and 9*B*).

Fig. 4.

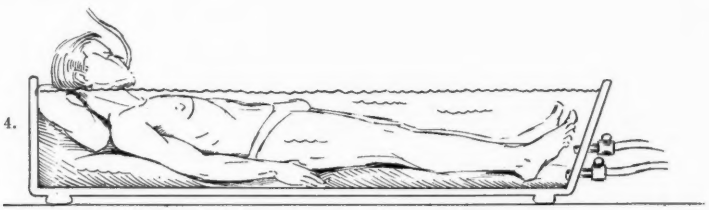


Fig. 5.

Fig. 6.

Fig. 4.—Induction of hypothermia by immersion in cold water.

Fig. 5.—Induction of hypothermia by packing the patient in cracked ice. While messy, this method is very effective. It is useful in treating hyperpyrexia from any cause. It is especially beneficial in the postoperative management of cyanotic patients, particularly if they are running a fever.

Fig. 6.—Use of a cold chamber ("deep freeze") to produce hypothermia. Because of the extreme coldness of the air, there is always danger of frostbite or gangrene of the extremities.

After the definitive surgery is completed the cold fluid is replaced by warm water and the patient is rewarmed to a level where respiration is spontaneous and adequate. This is usually at about 84° F. (28.8° C.). We have chosen

*Obtainable from the Thermo-Rite Products Corporation, 1748 Main St., Buffalo, N. Y.

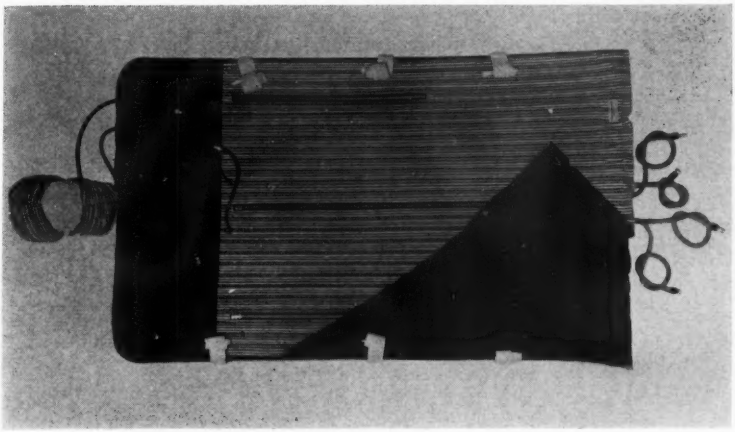


Fig. 7.—Rubber blanket with internal coils for the circulation of cold liquid provides the most satisfactory method of inducing hypothermia.

Fig. 8.—Compressor to provide circulation of either cool or warm (for rapid rewarming) fluids through the blanket.

to permit spontaneous (slow) rewarming to take place above this level. It is usually complete in about twelve hours, but full consciousness may return at any time.

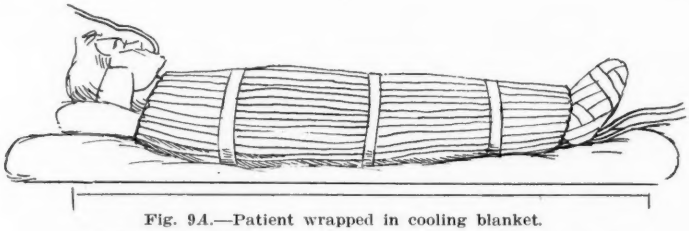


Fig. 9*A*.—Patient wrapped in cooling blanket.

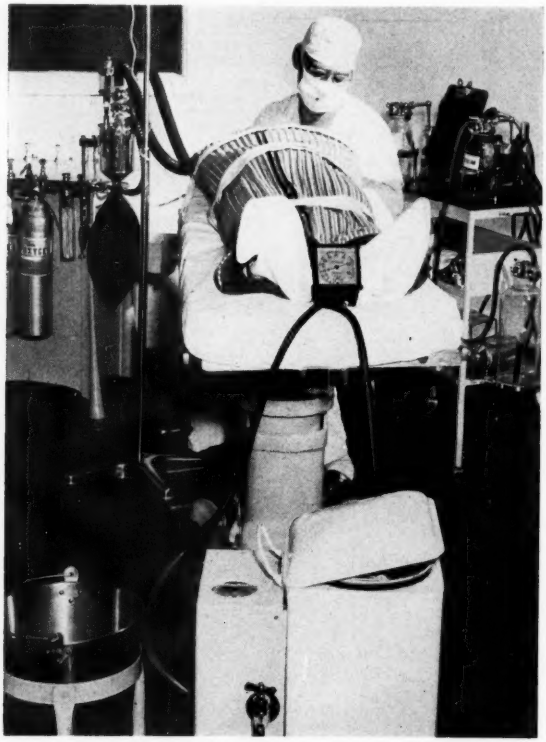


Fig. 9*B*.—Crude but inexpensive method of circulating cold brine through blanket by an ordinary water pump.

Temperatures are taken rectally (or vaginally) either by a mercury thermometer, or preferably by a thermocouple. A continuous recording thermocouple is very helpful.

Anesthesia is essential in inducing hypothermia both to render it painless and to reduce the tendency to shivering which retards the cooling.

Thiopental sodium and procaine are administered intravenously by the technique reported by Keown and his associates.[22] An endotracheal tube is

inserted and connected to a closed anesthesia system. A direct writing electrocardiograph is used to detect the electrical waves associated with shivering. Their appearance is an indication for the use of additional Pentothal Sodium. No attempt is made to produce a deep level of anesthesia. Frequently slight movements of the extremities occur even during the definitive portion of the surgery.

The anesthesiologist takes over respiration as soon as spontaneous efforts cease or become ineffective, usually between 80° and 85° F. This is rhythmically maintained by manual compression of the breathing bag except when the circulation is actually interrupted. At that point pulmonary inflation is useless and the movements of the respiratory organs may hamper the surgeon. As soon as the circulation is resumed the anesthesiologist again produces intermittent rhythmic lung inflation, continuing until spontaneous respiration returns and becomes adequate.

Constant observation of the electrocardiographic record is essential since ventricular asystole or fibrillation may occur at any time during the cooling process.

Adequate hypothermia may be established in infants within an hour. Older children take longer, and adults may take four hours or more. If the falling temperature stays at a given level for an hour or more, cracked ice may be poured into the blanket directly next to the patient's skin. This is apparently harmless and is quite effective in increasing the rate of cooling.

## SURGICAL TECHNIQUE

Surgery under hypothermia is very similar to that at normal body temperatures once the surgeon becomes accustomed to the cold feel of the tissues. Cold saline solution and cold wet sponges may cause a sense of strangeness to the members of the operating team.

Incisional bleeding is less profuse than at normal temperatures, but is at least as persistent. Ligation or electrocoagulation of bleeding points is just as essential for good hemostasis.

The heart feels warmer than the other tissues. It beats strongly although more slowly than usual.

Ventricular fibrillation may supervene at any time, seeming to occur more readily than at normal temperatures. Standstill is by no means rare. Since the time factors required for re-establishment of the circulation are by no means as critical as at normal temperatures, either manual cardiac massage or defibrillatory measures may be temporarily postponed or may be applied very deliberately.

Electric countershock is much more effective in producing defibrillation during hypothermia than at normal temperatures. It may therefore even be considered advisable to permit the heart to fibrillate throughout the definitive portions of the surgery. In the experimental laboratory we have sometimes deliberately induced standstill with acetylcholine or ventricular fibrillation by electric induction in order to ensure a quiet heart during the definitive maneuvers.

It is considered good practice in human surgery to interrupt the circulation for as short a period of time as possible rather than to utilize the maximum possible at the particular level of hypothermia. Our longest period of complete circulatory interruption with recovery when using an open technique was six and one-half minutes (M. A. F.). Our longest complete circulatory interruption with the closed technique was twenty-two minutes (K. C.). While the patient did not finally recover (cardiac standstill during postoperative bronchoscopy) there was no evidence of cerebral damage thirty hours after surgery.

Fig. 10.—Ease (and pathways) of production of air embolism to the systemic arteries after opening the left side of the heart, or after wide opening of a right cardiac chamber in the presence of a large septal defect. At the present time this great risk would seem to interdict the closure of atrial septal defects by an open technique.

It is now our practice routinely to administer a Gelatin-Ringer suspension of red cells directly into the aorta by way of a polythene tube throughout the period of circulation interruption (Fig. 2). We feel that this general arterial perfusion greatly lengthens the time of tolerable circulatory interruption and keeps the patient in much better condition during the actual surgery.

The usual thoracic operative incisions are the ones employed. Transection of the sternum and opening of both pleurae in the fourth interspace provide an ideal approach to the right side of the heart and the great blood vessels.

## INDICATIONS FOR HYPOTHERMIA

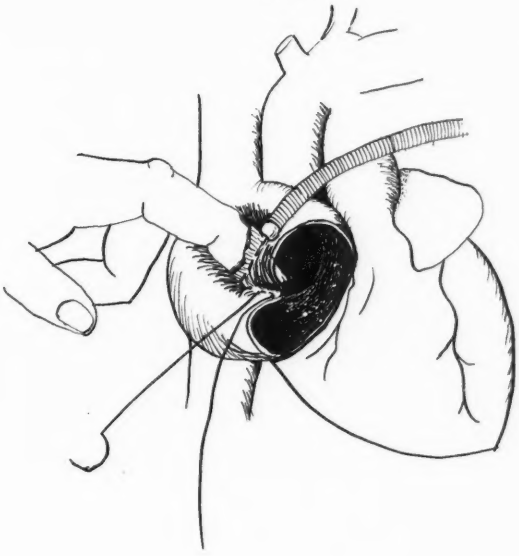
As a result of this small but intensively observed series of cases we have come to certain conclusions regarding the present indications for, and contraindications to, the use of hypothermia in cardiac surgery. We well realize that these considerations must change with progressive improvements which are to be expected as familiarity with this method increases.

At present we think hypothermia is indicated:

1. In infants:

   *A.* As an adjunct to orthodox surgery in severely cyanotic infants. Probably the optimum range of temperature in this type of case

Fig. 11.



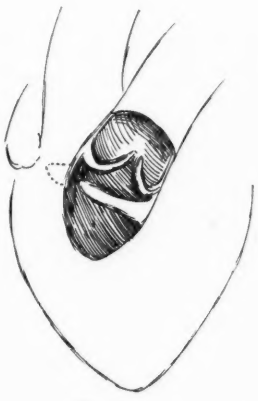


Fig. 12.

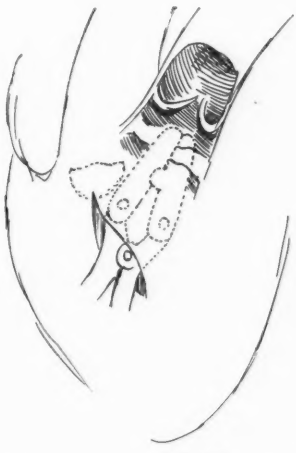


Fig. 13.

**Fig. 11.**—Technique of atrio-septo-pexy which is so safe and satisfactory that hypothermia and open surgery would seem contraindicated.

**Fig. 12.**—Essential defects in tetralogy of Fallot are pulmonic obstruction and high interventricular septal defect.

**Fig. 13.**—Direct resection of an obstructing supraventricular crest. Hypothermia facilitates and adds appreciably to the safety of orthodox surgery in patients with cyanotic heart disease.

would be 74° to 79° F. (23.3° to 26.1° C.). McQuiston[3] and Potts[4] have already reported this use of hypothermia although not at such low levels.

*B.* As a means of permitting direct surgical procedures upon the great blood vessels which involve interrupting the circulation to vital centers for prolonged periods of time. The optimum temperature range would probably be 70° to 76° F. (21.1° to 24.4° C.).

*C.* As a means of performing open intracardiac surgery within the chambers of the right heart under direct vision. Intra-arterial transfusion and operating under a level of Ringer solution may significantly aid the recovery.

2. Children: The same indications just mentioned; however, they are less suitable subjects.

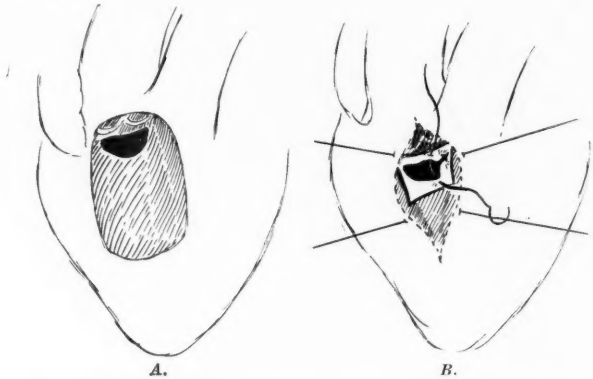



Fig. 14.—*A*, Typical high interventricular septal defect approached through a right ventricular incision as in M. A. F. *B*, Direct suturing of the defect. Use of a free patch of pericardium to reinforce the suture line is desirable.

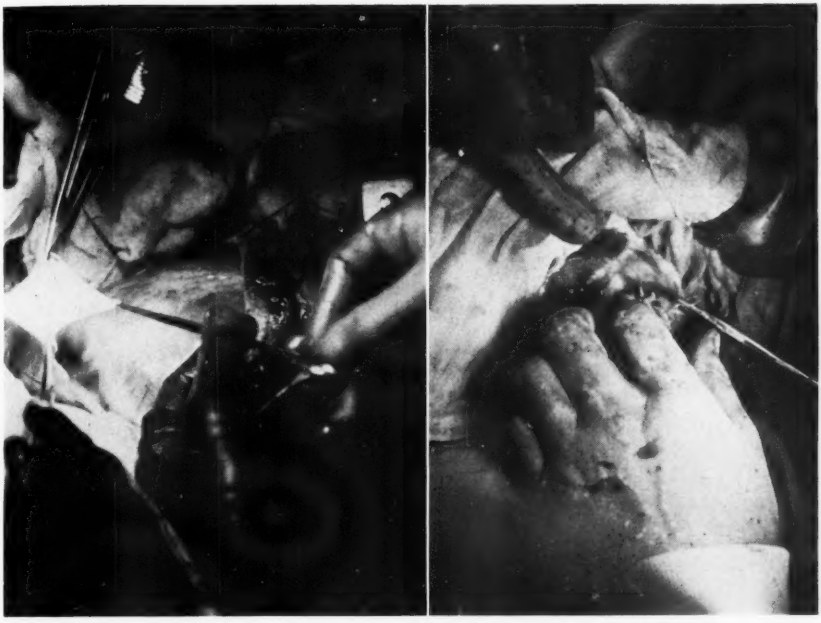
3. Adults: The same indications, but even less suitable. Body temperature should not be brought below 79° F. (26.1° C.).

### CONTRAINDICATIONS TO HYPOTHERMIA FOR CARDIAC SURGERY

1. Severe myocardial damage.
2. Acquired heart disease.
3. Left-sided lesions which require an open surgical technique.
4. Atrial septal defects, since safe and effective closed techniques (atrio-septo-pexy, and polythene bridging by use of a well) now exist. Opening the right atrium in the presence of an atrial septal defect is tantamount to opening the left atrium with its inherent risk of peripheral arterial air embolism (Fig. 10).

### SUMMARY

1. By the use of hypothermia we can safely interrupt the entire circulation for a period of time long enough to open the chambers of the right side of the heart and to perform direct intracardiac surgery.



*C.* *D.*

Fig. 14.—*C*, Application of the pericardial patch. *D*, Suturing of the defect.

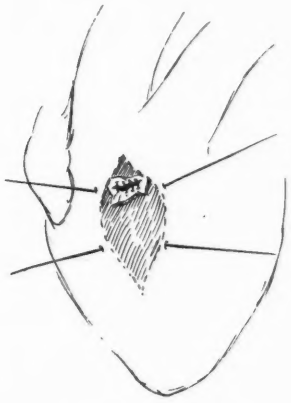


Fig. 14*E*.—Defect closed.

2. The present risk of arterial air embolism presently interdicts opening the left side of the heart and precludes safe use of an open technique for repair of large septal defects.

Unfortunately, at the present stage of developments we can only categorically establish the value of hypothermia as a valuable adjunct in the treatment of very cyanotic individuals with congenital heart disease.

We hope and believe that the case of M. A. F. points the way to the general application of hypothermia and direct suturing to small interventricular septal defects by the open technique (Fig. 11).

A logical extension of the consideration of these two probable uses would suggest the future simultaneous correction of both the pulmonic obstruction and the high interventricular septal defect (with an overriding aorta) in selected cases of tetralogy of Fallot. It is only by such a combined program that we can hope to restore the defective hearts of these unfortunate individuals to an essentially normal state (Figs. 12 to 14).

## CONCLUSIONS

1. Hypothermia is presently of little value in acquired cardiac lesions and in lesions of the left side of the heart.

2. Hypothermia is dangerous in adults since the myocardium may become fatally depressed.

3. Hypothermia and an open technique are dangerous in treating large septal defects because of the likelihood of air embolism.

4. Hypothermia is essentially useful in small children with congenital heart disease involving the right side.

5. Hypothermia greatly enhances the chance of recovery as an adjunct in the orthodox surgical treatment of very cyanotic children.

6. Hypothermia permits total interruption of the circulation for relatively long periods with complete recovery.

7. Hypothermia and open surgery are probably essential for the correction of ventricular septal defects.

8. Combining the success in the treatment of cyanotic lesions and that of interventricular septal defects one is led to the idea and hope of complete correction of the essential lesions existing in cases of tetralogy of Fallot.

9. Progressive improvements in technique and increased familiarity with hypothermia may eventually lead to its extensive use in permitting open intracardiac surgery for many conditions now treated by closed techniques at normal temperatures.

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## DISCUSSION

DR. F. J. LEWIS, Minneapolis.—I wish to thank the Association for the privilege of discussing Dr. Bailey's excellent presentation. At the University of Minnesota much of our experience with hypothermia, I am gratified to find, has been somewhat similar to Dr. Bailey's. We too have planned to use hypothermia both experimentally and in human beings largely to treat defects in which an open procedure would seem to be the essential or, at least, the most desirable method. Hence, we have been concerned primarily with auricular and ventricular septal defects.

In experimental animals, after some experience was gained, it has been relatively easy to make and, at a later operation, close large auricular septal defects. We have used a simple closure technique with a continuous silk stitch and no grafts. Coronary air embolism is avoided by outflow occlusion of the heart, plus rapid filling of the left chambers of the heart with saline solution at the time of right atrial closure. The problem of ventricular septal defects has, in our hands, been considerably more complicated. With hypothermia it is possible to produce ventricular septal defects experimentally, and close them, especially if the septal defects are made in the lower part of the ventricular septum. However, the high ventricular septal defects, one of which has been so brilliantly dealt with by Dr. Bailey, are, as most of us know, much more different to approach, for they are hidden by the tricuspid valve and intimately associated with the aortic and mitral valves as well. Hypothermia, however, does provide a method for producing such defects in dogs, a procedure that I feel is essential before we can take the next step of advocating its usage in human beings.

Whether hypothermia does establish itself ultimately as the best method of dealing with some of these intracardiac defects or not, it is, I think, at the present time a very adequate way of producing and closing a large number of intracardiac defects experimentally, utilizing what is essentially a simple technique. We find that an effective way

to cool animals which have an arteriovenous fistula has been advocated by Boerema; the blood is pumped from the dog's artery out through refrigerated coils and back into its vein. It is possible with very little danger to reduce the dog's body temperature to 25° C. within thirty minutes and proceed with an intracardiac operation. Following this the dog can be rewarmed rapidly in hot water or by immersing these coils in hot water, and the whole technique in the experimental laboratory can be completed in a relatively short time.

To date we have used hypothermia in the treatment of three patients with simple atrial septal defects. There was one death, a 46-year-old woman in congestive heart failure who, interestingly enough, developed an idioventricular rhythm with complete sinoatrial heart block during hypothermia. She did not recover from this conduction defect and despite the fact that the immediate clinical condition was excellent, the patient died suddenly and unexpectedly on the third postoperative day.

DR. SAMUEL KAPLAN, Cincinnati.—Earlier this afternoon Dr. Helmsworth mentioned our experimental observations with hypothermia during complete by-pass of the heart. It is well known that the young of most species tolerate a lower body temperature better than the fully grown adult of the same species. Therefore we extended our studies to hypothermia in newborn puppies and were able to reduce the rectal temperatures to 59° F. or 15° C. by placing the puppies in ice water. At this temperature the heart rate was reduced and we were able to confirm that there was marked reduction in the cardiac output. With this experimental background it appeared reasonable to use hypothermia to reduce or abolish hypoxia during the diagnostic study and surgical treatment of congenital cardiovascular anomalies in infants and children. It is stressed that this aid was only in desperately ill infants in whom hypoxia was evident.

To date, twenty-two patients between the ages of 18 days and 4 years have been subjected to hypothermia by surrounding the patient with polyethylene bags containing cracked ice. In the majority of patients the rectal temperature was reduced to 75° F. or 24° C. It took about twenty to thirty minutes to reduce the rectal temperature from the normal to 75° F. where it was maintained during the diagnostic study or operative procedure. The patients were rewarmed by placing them in a tub of water at 104° F. or by surrounding them with hot water bottles. During the hypothermic state the pulse and respiratory rates fell with the temperature. It is difficult to estimate the optimum temperature for surgical procedures in these desperately ill infants. The best guide has been the heart rate. When it reaches about 80 to 100 per minute, we believe the optimal temperature has been achieved. Further lowering of the rectal temperature may be associated with arrhythmias, especially heart block, which is preceded by prolongation of electrical systole. The placing of ice close to the skin has not produced any irreversible skin changes.

It has been said that hypothermia may be a narcotic agent in itself; although it is true that the amount of anesthetic agent required during the cooled state is small, we have repeatedly noted that the infants will cry and move at a temperature of 75° F. We have concluded that in infants and young children it is possible to reduce the body temperature to levels described without any harmful effects directly attributable to the hypothermic state. The object of hypothermia was to improve the physiologic state of the cardiovascular system because of reduction of general metabolism.

DR. WILLIAM H. MULLER, Los Angeles.—I certainly enjoyed Dr. Bailey's very interesting presentation. At the U.C.L.A. Medical Center we also have been interested in producing hypothermia in certain patients with congenital heart disease who are undergoing cardiovascular operation. Our interest arose because we had two untoward experiences during which irreversible central nervous system damage occurred and the patients died after the procedure.

Following the work of McQuiston and Potts, Bigelow, and others, we decided to try to lower the temperature slightly, or at least not allow it to rise during the procedure. Since there appeared to be certain advantages to actually reducing the temperature, we

have used hypothermia during the past fourteen months in twenty-five selected patients who had congenital heart disease. All were children, whose ages ranged from a few days to 17 years. Most of these patients were severely cyanotic or were in cardiac failure.

The method we have used is very similar to that mentioned by Dr. Kaplan, that is, the patient was placed on polyethylene bags filled with crushed ice after the anesthetic was begun. The rate of lowering depends on the size of the patient, but the desired temperature can usually be reached within from forty-five to ninety minutes. In most instances we have reduced the temperature to approximately 24° or 26° C. However, in two patients who had transposition of the aorta and pulmonary artery, and in whom we partially transposed the cardiac venous return in a manner very similar to that used by Dr. Lillehei and Dr. Varco, we lowered the temperature even more, 21.5° C. in one and 19.5° C. in the other.

Most of the patients have been followed with the electroencephalograph during the operation, and it showed greater changes in control patients than in those whose temperature had been lowered. It was felt that these changes were the result of having to use more anesthesia in the control patients. The electrocardiogram shows slowing of the pulse and prolongation of the PR interval and the QRS complex. However, ventricular fibrillation, which has been noted in dogs in which the temperature has been lowered, has not developed in any of our patients. On the contrary, we feel that there have been fewer serious arrhythmias than would have occurred if cooling had not been used. The blood pressure usually remains the same but may drop slightly. We have found no definite point at which the breathing ceases spontaneously. In some patients it has ceased at approximately 27° or 28° C. However, one patient whose temperature was lowered to 19° or 19.5° C. still breathed spontaneously. We have found that the arterial oxygen saturation in some cyanotic patients may rise considerably as a result of cooling alone. In one of the patients who had arterial transposition, the saturation rose from 7.8 to 19.7 volumes per cent, just as the result of cooling.

We are, at present, studying the electrolyte changes and the changes in blood clotting and blood constituents, but do not yet have sufficient data to draw conclusions. We raise the temperature in these patients by means of an electric blanket over a period of from one to three hours. The blanket is removed when the temperature reaches about 35° C.; and it usually returns to normal in two or three hours. We have had no difficulty with a compensatory hyperthermia. We have controlled shivering during this period by one of the curare-like drugs, the anesthesia having been discontinued. We have had no complications directly attributable to the hypothermia, and we feel that hypothermia certainly prolongs the operating time, reduces arrhythmias, and we think we have been able to get away with many procedures that would have been impossible otherwise.

Dr. Holman asked what success we had in the patients with transposition of the aorta and pulmonary artery. We have been able to transpose the superior vena cava and superior pulmonary vein in two out of six patients upon whom we attempted it. Most of these patients were only a few days or a few months old.

DR. CONRAD R. LAM, Detroit.—I should like to congratulate these pioneers who are working on the use of hypothermia, and to discuss one of the complications which has been mentioned and which resulted in the death of one of Dr. Bailey's patients. I refer to the condition called coronary air embolism. Some work we have done will be reported at another meeting by my associate, Dr. Geoghegan, but I think it is so important that it should be mentioned here. It is possible to administer a uniformly fatal dose of air, which is 1.5 c.c. per kilo, to a dog, and to reverse this in practically 100 per cent of the dogs. A little reasoning will assure us that a bubble of air cannot possibly be an embolus. It can pass through the capillary bed and we have demonstrated that such air can be collected in the coronary sinus. When the heart is failing from coronary air embolism and the bubbles in the vessels are visible, the aorta should be clamped and manual systole applied. This maneuver provides an adequate pressure in the coronary arteries so that the air is forced out and the cardiac musculature assumes a normal color. Obviously, before

doing this, the balance of the air in the ventricle should be removed by aspiration, otherwise there will be repetition of the coronary embolism. Resuscitation may be complicated by ventricular fibrillation, but the application of the electrical defibrillator will restore normal rhythm. Presumably, any air which has gone to the cerebral vessels would be forced out into the venous system also.

DR. ADRIAN LAMBERT, JR., New York.—I am impressed with this work and I would like to ask one or two questions, possibly because it is not quite clear to me what procedure Dr. Bailey has used. I should like to ask—and this may be redundant in that he may have answered it—whether he has been able to interrupt the arterial circulation to the head without getting permanent changes as a result of this interruption? Second, at what time interval will permanent changes in the brain develop after interrupting the return flow of blood from the head under conditions of hypothermia?

DR. BAILEY (Closing).—I had no idea there was so much cooling going on. I believe that Dr. Lewis and Dr. Varco were the first to successfully close an atrial septal defect by an open technique under hypothermia. It is quite easy, of course, to make and close interatrial defects in dogs. Usually air embolism is not a problem in experimentally created defects, and that is what probably misled us in human beings. However, it is different when you have one of these huge low defects such as a persistent ostium primum. At least our first patient did not do well by this open technique.

I do not know whether I brought out that adult patients do not do very well. Those with acquired heart disease such as aortic insufficiency and mitral insufficiency, and one adult with an auricular septal defect of this type, who was not operated on by an open technique but really by an extension of atrio-septo-pexy, all showed serious difficulty before the definitive surgery was even begun. One had ventricular fibrillation before that stage, and put us to the problem of trying to resuscitate the heart even while trying to correct the definitive defect. We are quite sure that adults with heart disease of an organic type, particularly of an acquired type, do not tolerate hypothermia very well.

## CASE REPORT

Actually, it was amazing how easily the defect could be closed in this child with the ventricular septal defect. The tricuspid valve was available, but it was not necessary to include it in the sutures as the edges of the defect came together very well. I think these high septal defects ordinarily are not associated with much lack of tissue. It is just a separation of the two edges and they can be sutured rather easily.

Dr. Kaplan has reported on Dr. Helmsworth's experience. He has really operated on a lot of people under hypothermia. I understand their patients were mainly children and I suppose they have avoided some of the problems we undertook. Certainly these desperately ill cyanotic patients do very well with conventional therapy with hypothermia. We have not found any constant temperature at which heart block develops; sometimes it develops at rather higher temperatures than would be expected. This is transient unless you actually pick up the atrioventricular conduction bundle with a suture, which can be done deliberately in animals but should be avoidable in human beings because it is characteristically located caudad to the ostium of the coronary sinus. I believe we should not have too much trouble with heart block.

Dr. Muller also has a tremendous series. Again I understand that it is largely composed of small children, many of them severely cyanotic. I am interested in the method that both he and Dr. Kaplan are using to cool these individuals, although it had seemed to us that the blanket was just about as good for an infant as for an adult. I am a little amazed that he has not had more trouble with ventricular fibrillation, because in our thirteen cases we had ventricular fibrillation in six. Two of them recovered with proper therapy, but they certainly had it, and I would imagine that this would occur in Dr. Muller's series too. I do not know whether there was a difference in the type of surgery performed. Perhaps more of his was extracardiac surgery. All of our operations were

intracardiac except in the transposition cases. I am not clear as to whether any of his patients were subjected to complete interruption of the circulation, which might be the reason for the difference in our experiences.

Certainly the arterial oxygen saturation does rise with cooling in these patients, and they become visibly pink whereas they have been perhaps almost black before the induction of hypothermia. I am quite certain that the method of Dr. Varco and the method Dr. Muller is using for the transposition of the great arteries, are sound. I am convinced that one cannot safely transpose the great arteries with any hope of eventual cure, so the only logical answer is to transpose the veins, since the right ventricle will probably be able to compete forever with the higher pressures of the aorta.

I am very much interested in Dr. Lam's report on the correction of coronary air embolism, because that certainly is something about which we should learn. Actually we have tried vigorous massaging of the heart. However, even in dogs we have not always been able to get the heartbeat back; in the two patients in our series in whom this occurred we certainly were not able to restore normal contractions. They did fibrillate and the fibrillation was persistent.

I am a little confused by Dr. Lambert's questions. Can we completely interrupt the arterial circulation to the brain without damage to the brain, and for how long? I suppose for twenty minutes or for whatever time you interrupt the entire circulation. I imagine he means at hypothermic levels. We have not specifically interrupted the cerebral circulation in either animals or human beings, but I would suppose that the interruption to the cerebral circulation would be nearly complete within a couple of minutes of clamping the venae cavae, and would last until the general circulation was restored. We have not investigated specifically either the venous drainage of the brain or the arterial supply to the brain, but have been able to use prolonged periods of obstruction of circulation in dogs at very low temperatures (16° C.), the maximum being around forty minutes without subsequent brain damage that we could detect. I believe that by perfusion of the aorta by the technique described, the period of vena caval obstruction could be significantly increased to perhaps an hour.

# THE MANAGEMENT OF THE DANGEROUSLY TORN AURICLE

WILLIAM K. SWANN, M.D. (BY INVITATION), THOMAS L. LOMASNEY, M.D. (BY INVITATION), AND JORGE RODRIGUEZ-ARROYO, M.D. (BY INVITATION)
KNOXVILLE, TENN.

THE UTILIZATION of the left auricular appendage as an avenue of approach to the diseased mitral valve was first done by Souttar[1] and later by Bailey[2] and Harken.[3] It has now been widely adopted in the treatment of mitral stenosis.

The operative procedure has been fairly well standardized and is described elsewhere.[4] The technique is relatively simple and the procedure is generally a safe one.

However, there are certain normal and pathologic variations in the auricle and its appendage which may render the procedure extremely hazardous. The auricular appendage may be so small that it does not easily permit introduction of the operative finger after amputation or wide opening of the appendage. This will require a lower and more unsafe application of the auricular clamp to the wall of the auricle itself. In the presence of a greatly enlarged auricle or an eccentric location of the mitral orifice, or both, manipulation by the operative finger either with or without a cutting instrument may create exceptional pressure or torsion at the site of the entrance into the auricle. The usually friable auricular tissue may become even more surgically unacceptable in the presence of adhesive pericarditis. It has been necessary to decorticate the auricle in three of our patients in whom this condition was found.

Any one or a combination of these factors may result in a tear in the auricle, and this tear may readily extend below the previously applied purse string.

The operator may or may not recognize when the tear has occurred. He may feel a relaxation or "giving-way" of the auricular wall about the finger; there may or may not be blood loss about the finger at this time. The operator should be prepared to deal with this tear of the auricular wall which is often simply handled by a lower application of the clamp as he withdraws the operative finger. If there is still leakage of blood below the reapplied clamp, a second clamp may be applied below the first one. A nesting group of clamps has been described for this purpose by Harken.[5] It is then a simple matter to remove the proximal clamps and oversew the torn auricle. There are, however, several dangers in the use of this method which are apparent when one considers the anatomic relations of the auricular appendage.

Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

## SURGICAL ANATOMY OF THE AURICULAR APPENDAGES

The importance of the anatomy of the auricular appendages has been emphasized for us after our experience with two patients undergoing intracardiac surgery in whom a tear of the auricle was produced. We feel that the original descriptions of this anatomy are not entirely adequate for present purposes. The following additions are based on dissections of twenty-four autopsy specimens.

The auricular appendages are the anterior prolongations of the auricles. They embrace, so to speak, the root of the great vessels, the right appendage bending around the aorta and the left around the pulmonary artery. They are both hollow and their darker color distinguishes them from the auricles proper.

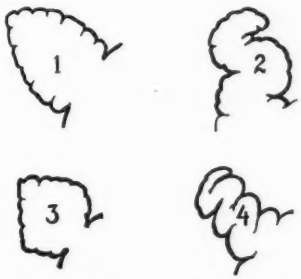



Fig. 1.—Variation in shape of the auricular appendages.

There are four usual shapes[6] (Fig. 1):

(1) Triangular
(2) S-shaped
(3) Rhomboidal
(4) Vermicular

On the left side the first two shapes are the most frequently found, the last two being found only occasionally. The right side is more constant, being almost always triangular.

The dimensions are variable but, in general, we can say that the left auricular appendage is longer and narrower than the right, and it presents a definite stricture at its base which is not found on the right side. Its length averages 4.5 cm., but it may vary from 2.5 cm. to 6.5 cm. The width varies from 1 cm. to 2.5 cm.[6]

The right appendage does not present any distinct line of demarcation from the auricle. It averages approximately 3.5 cm. in length, the width averages 2.5 cm.

The left auricular appendage is superimposed over the internal portion of the coronary sulcus and the superior portion of the interventricular sulcus. The appendage is separated from a constant vascular triangle by a layer of fatty tissue. This triangle is formed on two sides by the two branches of the left coronary artery—(1) the anterior descending branch, and (2) the circumflex branch—which meet the great cardiac vein on the third side of the

triangle (Fig. 2). Some of our dissections revealed two triangles due to a trifurcation of the left coronary artery (Fig. 3).

The right appendage covers the internal portion of the right coronary sulcus, overlapping it slightly. It is separated from the right coronary artery by fatty tissue.

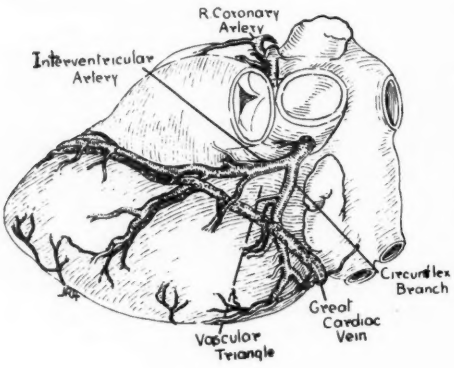



Fig. 2.

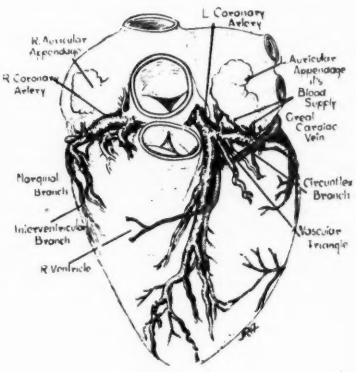
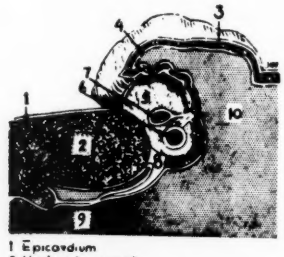



Fig. 3.

Fig. 2.—Vascular triangle in close proximity to left auricular appendage.
Fig. 3.—Variation of the vascular triangle caused by a trifurcation of left coronary artery.



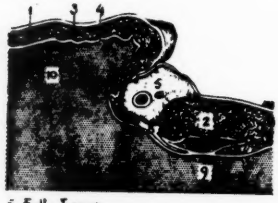




Fig. 4.—Cross-section reveals a part of the auricular wall is without epicardium and more susceptible to tearing or extension of a tear.

The blood supply of the appendage is provided by two branches of the circumflex artery, although sometimes only one branch is present. The veins are tributaries of the great cardiac vein. These vessels help to sustain the appendage in its position against the coronary sulcus, since, at the point where they reach the appendage, the epicardium is deflected and this provides the basis for dividing the appendage in two portions. One of these portions is covered by epicardium and the other is not. The latter area is in direct contact with the fatty covering of the coronary vessels in the coronary sulcus (Fig. 4).

The right appendage has no direct blood supply from the large vessels. This appendage is nourished by secondary divisions of the auricular vessels which arise from the right coronary artery. One of our specimens showed a vein of good size emptying in the base of the appendage. The right side presents the same two portions as the left, one covered by epicardium and the other uncovered.

The cavities of both appendages are a direct continuation of the auricular cavities, but there is a case mentioned by Blalock[7] in which the appendicular cavity did not exist.

## SURGICAL IMPLICATIONS

1. The stricture which is constant in the left side makes the passage of the finger through this appendage more difficult. Therefore a tear is more likely on the left side than on the right where there is no such stricture.

2. The tear is usually toward the coronary sulcus because of the direction of the pressure of the finger.

3. The portion of the appendage, namely, the base, which is not covered by epicardium is less resistant to tear.

4. In cases where the auricular appendages are too small to permit safe passage of the finger, an alternate approach must be used.

5. Due to the close relation of the left auricular appendage to the coronary artery and its branches and the great cardiac vein, care must be exercised to avoid suturing these vessels in case of tear of the left auricular appendage. Bailey[8] has reported a fatality when he divided a branch of the coronary artery from within the heart while using a guillotine knife.

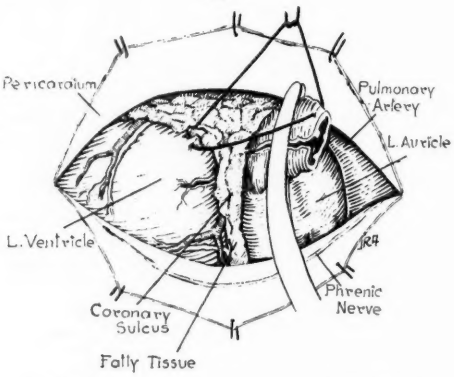
We have had occasion to manage dangerous auricular tears in two of our patients in our relatively small series of forty operative cases. We believe that a dangerously torn auricle can be repaired and the patient salvaged by attention to certain details. First, it is imperative to arrest hemorrhage from the auricle without damage to the coronary vessels. This entails a safe application of a clamp or a simple occlusion or compression of the opening by the hand of the operator. Second, preparation is then made to replace massive blood loss should it occur. We have used intra-aortic transfusion under pressure for this purpose. A suitable instrument should be on hand to clamp the descending aorta should this be necessary as an additional measure to insure the blood supply to the brain. Third, the auricular tear should be sutured without haste and with good visualization of suture placement.

## CASE REPORT

Mrs. B. D., a 39-year-old housewife, was admitted to Saint Mary's Memorial Hospital, Knoxville, Tenn., on July 1, 1952, with a complaint of dyspnea on exertion of three years' duration. She had become completely disabled for an entire year prior to this time. There was a past history of rheumatic fever in 1937.

Physical examination revealed the presence of ascites, ankle edema, and auricular fibrillation. A large pulmonary artery was observed at fluoroscopy but there was no enlargement of the left ventricle or of the left auricle. The over-all cardiac size was not appreciably increased. The auscultatory findings were consistent with a diagnosis of "pure mitral stenosis." Intensive medical treatment* resulted in loss of the edema and ascites, but attempts at converting the fibrillation were unsuccessful since the patient could not tolerate quinidine.

Fig. 5.



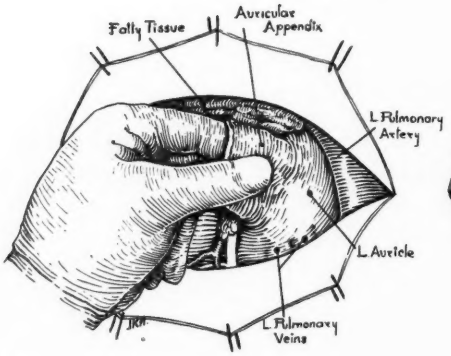




Fig. 6.

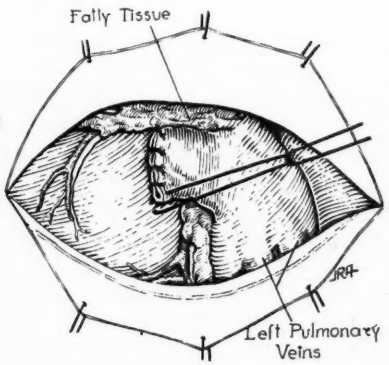



Fig. 7.

Fig. 5.—Tear in appendage extending to coronary sulcus.

Fig. 6.—Torn auricle occluded with two fingers and gentle compression of auricular wall against the ventricle.

Fig. 7.—Suture of torn appendage to ventricular muscle over the coronary sulcus.

Surgical correction of the mitral lesion was undertaken on Aug. 20, 1952. Exploration of the mitral valve through the usual approach revealed an extremely tight mitral stenosis (Type 1) but without calcification. In the course of producing a finger fracture of the anterolateral commissure, manipulation of the operative finger produced a tear in the small

*Directed by Doctor Robert J. Brimi.

auricular appendage. This tear was observed to progress down the side of the appendage on to the wall of the auricle with a small amount of blood loss at this time. The blood loss could be prevented by approximating the thumb against the index finger over the area of the tear in the wall of the auricle. As the operative finger was withdrawn from the appendage an effort was made to tent up the auricular wall by grasping the appendage between the thumb and the index finger and thus permit a lower application of the clamp. In spite of this maneuver when the clamp was closed it was observed that the tear in the auricle extended below the level of application of the clamp (Fig. 5). Several reapplications of the clamp were necessary to prevent continued bleeding. With the lowest application of the clamp it was observed that the instrument was in contact with the fatty tissue overlying the coronary vessels in the sulcus. An attempt was made to oversew the appendage distal to the clamp but in doing so this tissue was partially avulsed, possibly due to repeated applications of the clamp to the friable auricular tissue.

A maneuver was then deliberately adopted which consisted of insertion of two fingers of the left hand back into the auricle as the clamp was removed. The wall of the auricle was compressed at the same time against the fingers by the thumb of the left hand. This "two fingers in the dike maneuver" resulted in complete arrest of the hemorrhage (Fig. 6).

This situation was maintained until the blood previously lost had been replaced through the usual venous routes and preparation was made for rapid replacement of blood in anticipation of its loss during definitive closure of the torn auricle. A No. 16 needle was introduced into the aorta and suitable arrangements made to give the blood under pressure. After a few minutes the patient had completely recovered from the initial blood loss, and it was elected to repair the defect by turning the auricular wall and what remained of the auricular appendage downward over the coronary sulcus and suturing the torn auricle to the ventricular muscle (Fig. 7). Interrupted mattress sutures of fine silk on atraumatic needles were used for this purpose. The sutures in the ventricular muscle were placed at right angles to the direction of the fibers to prevent avulsion of muscle. Because of the low pressure in the auricle, tight sutures or continuous sutures were not necessary for this purpose. Care was taken to avoid branches of the coronary artery. Active bleeding occurred during this maneuver, but perfect visualization was maintained throughout by adequate suction apparatus and the patient's condition was prevented from further deterioration by giving 700 c.c. of blood under pressure directly into the aorta. After completion of the auricle-to-ventricle suture the area was covered with a small strip of Gelfoam sponge and the pericardium was sutured snugly over the repair.

At the termination of the operation the blood pressure was 70/40 but shortly thereafter was above 100 systolic. Thereafter the postoperative course was not particularly remarkable and the patient was discharged home on Sept. 12, 1952. At the present time she is able to do light housework without exertional dyspnea.

## SUMMARY

In a series of forty mitral valve commissurotomies, two instances of hemorrhage from a dangerously torn auricle were encountered. One of these cases is described in detail together with a method of managing this emergency.

It is emphasized that the surgeon in his haste to arrest hemorrhage from the torn auricle may possibly create an irreversible situation by application of the clamp across the coronary vessels. The application of clamps without perfect vision is therefore inadvisable.

Blood loss can be controlled by occlusion or compression of the torn auricle with the operative hand while preparations are then made for rapid intra-aortic blood replacement before definitive closure of the defect is attempted. These tears can then be managed safely under direct vision. Dangerous, ill-advised, and hasty maneuvers are to be avoided.

## ADDENDUM

Since preparation of this manuscript a similar method for managing this surgical emergency has been described by C. P. Bailey, H. E. Bolton, and H. P. Redondo-Ramirez.

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## DISCUSSION

DR. ROLLINS HANLON, St. Louis.—I have enjoyed this presentation of Dr. Swann and his associates and would like to emphasize one point which we have found important in handling the left auricle. Everyone realizes that it is inadvisable to apply a clamp very low down on the auricle, and this is unlikely to occur except in the face of severe bleeding due to a tear. On the other hand, with a small fibrotic auricle, one may occasionally make an injudicious application of the clamp even in the absence of bleeding.

When the clamp on the auricle compresses the coronary artery, the result may be ventricular fibrillation. It is helpful to have some warning of the onset of this complication before it is detected by inspection of the heart. Drs. J. G. Mudd and J. Inkley of the Division of Cardiac Catheterization have pointed out an electrocardiographic sign which has been useful to us in the operating room in detecting incipient ventricular fibrillation. We employ a continuous oscilloscopic recording of the cardiac action which is periodically transferred to a recording electrocardiograph.

(Slide.) This shows the normal activity of the heart before surgery was begun, followed by the defect in the electrocardiogram which indicates impending ventricular tachycardia or fibrillation, namely, the high takeoff of the S-T segment. When this change is seen, it calls for immediate reapplication of the clamp or a prompt shift in its position. As seen in the other parts of the tracing, this initial change in the electrocardiogram went from ventricular tachycardia into ventricular fibrillation.

(Slide.) In this instance, the heart was defibrillated promptly by simply changing the position of the clamp without the necessity for electrical defibrillation. In this tracing, a regular complex can be seen following closely after the ventricular fibrillation although some evidence of injury persists. The tracing had reverted to normal, as can be seen, at the end of the operation.

By watching closely for this high takeoff of the S-T segment during manipulation of the auricle, the surgeon should receive considerable assistance in the avoidance or prompt treatment of ventricular fibrillation.

DR. SWANN (Closing).—I would like to thank Dr. Hanlon for his discussion. The manuscript contains an addendum on a similar method of handling auricular tears that has been described by Dr. Bailey and his associates since our abstract was submitted.

# CYSTIC HYGROMA OF THE NECK ARISING AFTER THORACOPLASTY

EMIL ROTHSTEIN, M.D.,* AND EDWARD B. GALL, M.D.**
DAYTON, OHIO

CYSTIC hygroma is a benign, endothelial-lined, multilocular cystic tumor of lymphangitic origin. A review[1] of twenty cases of cervical hygroma treated at Johns Hopkins Hospital from 1936 to 1946 was made by Ward and his associates. They found that 93 per cent of all hygromas occur in the neck. The etiology is unknown but it is surmised that the cystic cavities are formed by a widening of normal lymph spaces. In the John Hopkins group fifteen of the twenty were male patients; sixteen were noted before the age of 10 years, and sixteen occurred on the left side of the neck. Two of their patients were adults; in one the hygroma started at age 26 and the other at age 41 years.

This report deals with the development of cystic hygroma in the neck of a 39-year-old man, three months after a thoracoplasty.

## CASE REPORT

L. W., a 39-year-old man, had been ill with pulmonary tuberculosis since 1944. An anterior right thoracoplasty (three ribs) was done Feb. 14, 1949, an anterior Monaldi drainage on March 8, 1949, and a posterior thoracoplasty (four ribs) on March 16, 1949. The next stage of surgery was delayed because of a chronic draining infection of the posterior thoracoplasty incision.

In June, 1949, the patient noted a small swelling in the right supraclavicular region. This gradually increased so that by March, 1950, it was approximately 8 cm. in diameter (Fig. 1). The only symptom was slight discomfort upon swallowing, possibly due to pressure upon the esophagus. The swelling was soft and fluctuant. There was no tenderness, redness, or induration. The mass was compressible to some degree but could not be made to disappear by means of pressure. It was dull to percussion; no breath sounds or murmurs were audible over it. Upon forced expiration with the glottis closed the structure became somewhat more prominent.

Upon x-ray examination (Fig. 2) the mass was seen to be opaque. Esophagram and bronchogram both failed to reveal significant findings.

The mass was explored (E. B. G.) on June 28, 1950. A cystic mass about the size of a grapefruit was found beneath the subcutaneous tissue, lying below the trapezius muscle superiorly and projecting below the clavicle anteriorly. No definite pedicle could be found nor was it in direct communication with any formed lymphatic or other vascular structures. It was removed in toto.

The cyst was filled with a cloudy white fluid. Examination of this fluid revealed 5 per cent protein with 19,100 cells, 100 per cent of which were lymphocytes. Smear and culture were negative for tubercle bacilli and other organisms. Microscopic examination revealed large cavernous spaces lined with endothelium. Some spaces were engorged with red corpuscles; the majority were empty. The cyst walls were of connective tissue with

From the Veterans Administration Center, Dayton, Ohio, and the University of Cincinnati College of Medicine, Cincinnati, Ohio.

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*Formerly Chief, Tuberculosis Service, Veterans Administration Center, Dayton, Ohio, and Instructor in Medicine, College of Medicine, University of Cincinnati, Cincinnati, Ohio, and now Chief, Tuberculosis Service, Veterans Administration Hospital, Brockton, Mass.

**Thoracic Surgeon, now Consulting Surgeon, Veterans Administration Center, Dayton, Ohio.

Fig. 1.—Cystic hygroma can be seen presenting subcutaneously in the right supraclavicular region.

Fig. 2.—Roentgenogram revealing radiopaque character of the cystic hygroma.

numerous small papilliferous projections extending from the lining. These were engorged with lymphocytes and contained lymphatic channels. The pathologic diagnosis was hygroma.

The postoperative course was uneventful and no recurrence was noted during the following two years.

## DISCUSSION

Two points of interest are raised by this case. The first of these deals with the preoperative differential diagnosis. A soft, nontender mass arising in the neck after thoracoplasty was a unique experience for us. Certain conditions were considered which were unrelated to the previous surgery, such as lymphoma, tuberculous glands, etc., but seemed ruled out by the soft, fluctuant, compressible character of the lesion.

Herniation of the lung was considered but was ruled out by the opacity of the lesion upon x-ray examination, by the failure to fill the lesion by means of bronchography, and because of the fact that preoperatively the right upper lobe had appeared totally diseased by consolidation and cavitation.

Arteriovenous aneurysm was suggested but was ruled out by the absence of a murmur or thrill and by the fact that the lesion, while compressible, could not be completely obliterated, indicating that the fluid it contained was not in free communication with the vascular system. The preoperative diagnosis of hygroma was accurately made based upon the known behavior of this lesion plus the differential diagnostic features mentioned.

The second point of interest deals with the possible relationship between the surgical procedure and the development of the hygroma. This is a lesion of unknown etiology and has not previously been identified with the postoperative course of thoracic surgery. Other cases have been reported, though rarely, in adults of this patient's age. Yet we are intrigued by the thought that the anterior and, later, posterior right upper thoracic surgery might in some way have affected the anatomy or physiology of the right lymphatic duct so as to give an impetus to the perhaps latent potentialities of hygroma development in this individual.

## SUMMARY

Approximately three months after right upper anterior and posterior thoracoplasty, a soft cystic tumefaction appeared in the right side of the neck of a 39-year-old patient. This was removed about one year later and was found to be a cystic hygroma. The differential diagnosis and the possibility of a relationship between thoracoplasty and hygroma are briefly discussed.

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# Announcement

## THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

### Notice of Annual Meeting

The 34th annual meeting of the American Association for Thoracic Surgery will be held May 3, 4, and 5, 1954, in Montreal, Que., Canada. Headquarters will be at the Sheraton-Mount Royal Hotel.

### Requests for Hotel Reservations

These should be mailed *directly* to the Reservation Manager, Sheraton-Mount Royal Hotel, Montreal, Que., Canada. Please mention this Association, type of accommodation desired, date, and approximate hour of arrival. If accommodations are desired elsewhere, please communicate directly with hotel of your choice.

### Thoracic Surgical Forum

After due consideration, the Council has decided to try an experiment by assigning one morning session to a "Thoracic Surgical Forum" for the presentation of short papers on current thoracic research, anatomy, modified surgical techniques, etc. Papers at this session will be limited sharply to ten minutes (including the showing of lantern slides or other illustrative material) with three minutes as the maximum discussion of each paper.

These papers will be published together in one issue of THE JOURNAL OF THORACIC SURGERY. Maximum length: 3,000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

### Abstracts for Papers

Abstracts for the presentation of papers at the 1954 meeting, including papers before the Forum, must be received on or before January 1, 1954, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Forum" or "For Regular Program."

*Five, repeat five,* copies of each abstract should be sent to the Secretary of the Association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

### Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Jan. 1, 1954, to be considered for action in Montreal. Applications received beyond this deadline will be deferred for consideration until 1955.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the sponsoring statement on the application form, the sponsors *must* submit a separate letter concerning the applicant direct to Dr. Lyman H. Brewer, III, Chairman of the Membership Committee, 2010 Wilshire Blvd., Los Angeles, Calif. Completed application forms should likewise be sent to Dr. Brewer. These regulations are at the direction of the Council and were made effective in 1952 at Dallas.